L3 ANSWER 1 OF 12 USPATFULL on STN
AN 2003:194142 USPATFULL
TI D-alanine racemase mutants of mycobacteria and uses therefore
IN Barletta, Raul G., Lincoln, NE, UNITED STATES
Barletta-Chacon, Ofelia, Lincoln, NE, UNITED STATES
PI US 2003133952 A1 20030717
US 6929799 B2 20050816
AI US 2002-323351 A1 20021218 (10)
PRAI US 2001-341485P 20011218 (60)
DT Utility
FS APPLICATION
LREP STINSON MORRISON HECKER LLP, ATTN: PATENT GROUP, 1201 WALNUT STREET, SUITE 2800, KANSAS CITY, MO, 64106-2150
CLMN Number of Claims: 17
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 1398
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention is directed to D-alanine racemase mutants of mycobacterial species. The D-alanine racemase gene (alrA) is involved in the systhesis of D-alanine, a basic component of peptidoglycan that forms the backbone of the bacterial cell wall. The present invention is also directed to methods of making live-attenuated vaccines against pathogenic mycobacteria using such alrA mutants and to the vaccines made according to such methods. The present invention is further directed to use of alrA mutants in methods for screening antimycobacterial agents that are synergistic with peptidoglycan inhibitors. Finally, the present invention is directed to methods to identify new pathways of D-alanine biosynthesis for use in developing new drugs targeting peptidoglycan biosynthesis in mycobacteria and to identify vaccines useful against pathogenic mycobacteria.

L3 ANSWER 2 OF 12 USPATFULL on STN
AN 2003:146354 USPATFULL
TI Insertional mutations in mycobacteria
IN Jacobs, William R., JR., City Island, NY, UNITED STATES
Bloom, Barry, Hastings-on-Hudson, NY, UNITED STATES
Kalpana, Ganjam V., Yonkers, NY, UNITED STATES
Cirillo, Jeffrey D., Mountain View, CA, UNITED STATES
McAdam, Ruth, Near Hatfield, UNITED KINGDOM
PI US 2003100100 A1 20030529
US 6752994 B2 20040622
AI US 2001-898762 A1 20010703 (9)
RLI Continuation of Ser. No. US 1997-850977, filed on 5 May 1997, PENDING Continuation of Ser. No. US 1994-247711, filed on 23 May 1994, ABANDONED Continuation-in-part of Ser. No. US 1994-190240, filed on 1 Feb 1994, ABANDONED Continuation of Ser. No. US 1991-806706, filed on 12 Dec 1991, ABANDONED Continuation-in-part of Ser. No. US 1991-714656, filed on 13 Jun 1991, ABANDONED
DT Utility
FS APPLICATION
LREP Craig J. Arnold, Amster, Rothstein & Ebenstein, 90 Park Avenue, New York, NY, 10016
CLMN Number of Claims: 30
ECL Exemplary Claim: 1
DRWN 29 Drawing Page(s)
LN.CNT 1691
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A mutated mycobacterium selected from the class consisting of mutated M. bovis-BCG, mutated M. tuberculosis, and mutated M. leprae. The mutation of M. bovis-BCG, M. tubeiculosis, or M. leprae is preferably effected through an insertional mutation of a mycobacterial gene. The insertional mutagenesis may be effected, for example, through illegitimate recombination or by a mycobacterial transposon. Such mutated

mycobacteria may then be transformed with an expression vector(s) containing a complement gene to the gene which is mutated, and preferably also including a heterologous gene.

L3 ANSWER 3 OF 12 USPATFULL on STN
AN 2003:136957 USPATFULL
TI Insertional mutations in mycobacteria
IN Jacobs, Jr., William R., City Island, NY, United States
Bloom, Barry, Hastings-on-Hudson, NY, United States
Kalpana, Ganjam V., Yonkers, NY, United States
Cirillo, Jeffrey D., Mountain View, CA, United States
McAdam, Ruth, Essendon, UNITED KINGDOM
PA Albert Einstein College of Medicine of Yeshiva University, Bronx, NY, United States (U.S. corporation)
PI US 6566121 B1 20030520
AI US 1997-850977 19970505 (8)
RLI Continuation of Ser. No. US 1994-247711, filed on 23 May 1994, now abandoned Continuation-in-part of Ser. No. US 1994-190240, filed on 1 Feb 1994, now abandoned Continuation of Ser. No. US 1991-806706, filed on 12 Dec 1991, now abandoned Continuation-in-part of Ser. No. US 1991-714656, filed on 13 Jun 1991, now abandoned
DT Utility
FS GRANTED
EXNAM Primary Examiner: Swartz, Rodney P
LREP Amster, Rothstein & Ebenstein
CLMN Number of Claims: 4
ECL Exemplary Claim: 1
DRWN 40 Drawing Figure(s); 29 Drawing Page(s)
LN.CNT 1746
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A mutated mycobacterium selected from the class consisting of mutated M.bovis-BCG, mutated M.tuberculosis, and mutated M. leprae. The mutation of M.bovis-BCG, M.tuberculosis, or M. leprae is preferably effected through an insertional mutation of a mycobacterial gene. The insertional mutagenesis may be effected, for example, through illegitimate recombination or by a mycobacterial transposon. Such mutated mycobacteria may then be transformed with an expression vector(s) containing a complement gene to the gene which is mutated, and preferably also including a heterologous gene.

L3 ANSWER 4 OF 12 USPATFULL on STN
AN 2002:272910 USPATFULL
TI Mycobacterial isocitrate lyase gene and uses thereof
IN McKinney, John D., Bronx, NY, UNITED STATES
Jacobs, William R., JR., City Island, NY, UNITED STATES
PI US 2002151031 A1 20021017
US 6733761 B2 20040511
AI US 2001-29715 A1 20011220 (10)
RLI Continuation of Ser. No. US 1998-54680, filed on 3 Apr 1998, GRANTED, Pat. No. US 6387694
DT Utility
FS APPLICATION
LREP Craig J. Arnold, Esq., Amster, Rothstein & Ebenstein, 90 Park Avenue, New York, NY, 10016
CLMN Number of Claims: 40
ECL Exemplary Claim: 1
DRWN 8 Drawing Page(s)
LN.CNT 1103
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention provides a purified and isolated nucleic acid encoding mycobacterial isocitrate lyase, as well as mutated forms of the nucleic acid. Further provided are purified and isolated isocitrate lyase proteins and mutated isocitrate lyase proteins. Additionally, the present invention provides vectors which comprises nucleic acid

sequences encoding mycobacterial isocitrate lyase and mutated forms of this nucleic acid, as well as host cells containing these vectors. Also provided is a mycobacterium containing one or more mutations in its isocitrate lyase gene. Further provided by the present invention are agents that inhibit the activity or expression of a mycobacterial lyase protein, a method of identifying these, and a method of producing them. Finally, the present invention also provides a method of identifying genes required for persistence of mycobacteria.

L3 ANSWER 5 OF 12 USPATFULL on STN
AN 2002:148581 USPATFULL
TI Antibiotic hypersusceptibility mutations in bacteria
IN Neyfakh, Alexander A., Chicago, IL, UNITED STATES
Vazquez-Laslop, Nora, Riverforest, IL, UNITED STATES
PI US 2002076722 A1 20020620
AI US 2001-950319 A1 20010910 (9)
PRAI US 2000-232579P 20000913 (60)
DT Utility
FS APPLICATION
LREP FULBRIGHT & JAWORSKI L.L.P., A REGISTERED LIMITED LIABILITY PARTNERSHIP, SUITE 2400, 600 CONGRESS AVENUE, AUSTIN, TX, 78701
CLMN Number of Claims: 36
ECL Exemplary Claim: 1
DRWN 10 Drawing Page(s)
LN.CNT 1887
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention discloses methods for identifying loci of antibiotic hypersusceptibility mutations using random insertional mutagenesis of a bacterial population with a selectable or screenable marker, treatment of a mutagenized bacterial population with an antibacterial agent, and selection of DNA of cells affected by the antibacterial agents. In some embodiments, the DNA selected is released from bacteria lysed in response to antibacterial treatment. The selected DNA also may be released as a result of exposure to a non-lysing antibacterial agent in combination with one or more additional treatments that results in bacterial lysis. In other instances, selected DNA may be released from bacteria only as a result of insertion of a lysis gene cassette through genetic engineering of the bacteria. In some instances, the selected DNA is used to transform fresh populations of bacteria and the cycle of DNA selection and transformation is repeated as many times as needed for obtaining hypersusceptibility mutants. After the DNA of such a mutant is collected, purified and sequenced, the location of a selectable or screenable marker identifies the antibacterial hypersusceptibility locus. The proteins encoded by these loci can serve as targets for potentiators of an antibacterial agent.

L3 ANSWER 6 OF 12 USPATFULL on STN
AN 2002:126349 USPATFULL
TI Identification of virulence determinants
IN Barletta, Raul G., Lincoln, NE, UNITED STATES
Harris, N. Beth, Lincoln, NE, UNITED STATES
PI US 2002064861 A1 20020530
AI US 2001-759287 A1 20010111 (9)
PRAI US 2000-175433P 20000111 (60)
DT Utility
FS APPLICATION
LREP SENNIGER POWERS LEAVITT AND ROEDEL, ONE METROPOLITAN SQUARE, 16TH FLOOR, ST LOUIS, MO, 63102
CLMN Number of Claims: 53
ECL Exemplary Claim: 1
DRWN 2 Drawing Page(s)
LN.CNT 1276
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Disclosed are methods for the determination of virulence determinants in

bacteria and in particular bacteria of the genus Mycobacterium. Also disclosed are compositions and methods for stimulating an immune response in an animal using bacteria and virulence determinants identified by the methods of the present invention.

L3 ANSWER 7 OF 12 USPATFULL on STN
AN 2002:303878 USPATFULL
TI Bacteriophage, a process for the isolation thereof, and a universal growth medium useful in the process thereof
IN Agrawal, Pushpa, Chandigarh, INDIA
Soni, Vishal, Chandigarh, INDIA
PA Council of Scientic and Industrial Research, New Delhi, INDIA (non-U.S. corporation)
PI US 6482632 B1 20021119
AI US 1999-295851 19990421 (9)
RLI Continuation-in-part of Ser. No. US 1999-277916, filed on 29 Mar 1999, now abandoned
DT Utility
FS GRANTED
EXNAM Primary Examiner: Mosher, Mary E.
LREP Ladas & Parry
CLMN Number of Claims: 33
ECL Exemplary Claim: 1,9
DRWN 1 Drawing Figure(s); 1 Drawing Page(s)
LN.CNT 1316
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention provides a isolated bacteriophage useful as a tool for studying biological, biochemical, physiological and genetic properties of actinomycetes and other organisms which comprises a novel strain of Saccharomonospora having certain specified characteristics. The invention also relates to a process for the isolation of the said bacteriophage and/or DNA phage and to a novel universal growth medium which is particularly useful in the said process. Another embodiment of the process relates to a cloning vector which comprises a plasmid or bacteriophage comprising the phage DNA of the invention.

L3 ANSWER 8 OF 12 USPATFULL on STN
AN 2001:157804 USPATFULL
TI Dim mutants of mycobacteria and use thereof
IN Cox, Jeffery S., Larchmont, NY, United States
Jacobs, Jr., William R., City Island, NY, United States
PA Albert Einstein College of Medicine of Yeshiva University, Bronx, NY, United States (U.S. corporation)
PI US 6290966 B1 20010918
AI US 1999-350326 19990709 (9)
DT Utility
FS GRANTED
EXNAM Primary Examiner: Swart, Rodney P.
LREP Amster, Rothstein & Ebenstein
CLMN Number of Claims: 16
ECL Exemplary Claim: 1
DRWN 8 Drawing Figure(s); 6 Drawing Page(s)
LN.CNT 588
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Disclosed are novel recombinant mutant strains of mycobacteria that are deficient for the synthesis or transport of dimycoserosalphthiocerol ("DIM"). The present invention also provides a method of producing a recombinant mutant mycobacterium that is deficient for the synthesis or transport of DIM, comprising mutating a nucleic acid responsible for the synthesis or transport of dimycoserosalphthiocerol, including a nucleic acid comprising the promoter for the pps operon, fadD28 or mmpL7. The present invention also provides a vaccine comprising a DIM mutant mycobacterium of the present invention, as well as a method for the treatment or prevention of tuberculosis in a subject using the vaccine.

L3 ANSWER 9 OF 12 USPATFULL on STN
AN 2001:59388 USPATFULL
TI Recombinant mycobacteria auxotrophic for diaminopimelate
IN Pavelka, Jr., Martin S., Bronx, NY, United States
Jacobs, Jr., William R., City Island, NY, United States
PA Albert Einstein College of Medicine of Yeshiva University, Bronx, NY, United States (U.S. corporation)
PI US 6221364 B1 20010424
AI US 1996-747177 19961112 (8)
DT Utility
FS Granted
EXNAM Primary Examiner: Minnifield, Nita
LREP Amster, Rothstein & Ebenstein
CLMN Number of Claims: 9
ECL Exemplary Claim: 1
DRWN 7 Drawing Figure(s); 7 Drawing Page(s)
LN.CNT 1347
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention refers in general to novel recombinant mycobacteria that are auxotrophic for diaminopimelate. In particular, this invention relates to novel auxotrophic recombinant mycobacteria, to methods of making the mycobacteria, and to uses of the mycobacteria to deliver vaccines. This invention also provides for uses of the mycobacteria in drug screening processes.

L3 ANSWER 10 OF 12 USPATFULL on STN
AN 1999:155521 USPATFULL
TI L5 shuttle phasmids
IN Jacobs, William R., City Island, NY, United States
Hatfull, Graham F., Pittsburgh, PA, United States
Bardarov, Stoyan, Bronx, NY, United States
McAdam, Ruth, Essendon, United Kingdom
PA Albert Einstein College of Medicine of Yeshiva University, Bronx, NY, United States (U.S. corporation)
University of Pittsburgh, Pittsburgh, PA, United States (U.S. corporation)
PI US 5994137 19991130
AI US 1998-75904 19980511 (9)
RLI Continuation of Ser. No. US 1994-247901, filed on 23 May 1994, now patented, Pat. No. US 5750384, issued on 12 May 1998 which is a continuation-in-part of Ser. No. US 1993-57531, filed on 29 Apr 1993, now abandoned which is a continuation-in-part of Ser. No. US 1992-833431, filed on 7 Feb 1992, now abandoned
DT Utility
FS Granted
EXNAM Primary Examiner: Degen, Nancy; Assistant Examiner: Schwartzman, Robert
LREP Amster, Rothstein & Ebenstein
CLMN Number of Claims: 9
ECL Exemplary Claim: 1
DRWN 21 Drawing Figure(s); 18 Drawing Page(s)
LN.CNT 2996
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB This invention is directed to L5 shuttle phasmids capable of delivering foreign DNA into mycobacteria and to methods of producing L5 shuttle phasmids. In addition, this invention is directed to a method of generating mycobacterial mutations and to a method of producing mycobacterial vaccines.

L3 ANSWER 11 OF 12 USPATFULL on STN
AN 1999:132589 USPATFULL
TI TM4 conditional shuttle phasmids and uses thereof
IN Jacobs, Jr., William R., City Island, NY, United States
Bardarov, Stoyan, Bronx, NY, United States

Hatfull, Graham F., Pittsburgh, PA, United States
PA Albert Einstein College of Medicine of Yeshiva University, Bronx, NY, United States (U.S. corporation)
University of Pittsburgh, Pittsburgh, PA, United States (U.S. corporation)
PI US 5972700 19991026
AI US 1997-938059 19970926 (8)
DT Utility
FS Granted
EXNAM Primary Examiner: Ketter, James; Assistant Examiner: Yucel, Irem
LREP Amster, Rothstein & Ebenstein
CLMN Number of Claims: 10
ECL Exemplary Claim: 1
DRWN 5 Drawing Figure(s); 3 Drawing Page(s)
LN.CNT 873
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention provides a conditional shuttle phasmid constructed by inserting a cosmid into a non-essential region of the TM4 mycobacteriophage that introduces DNA of interest into mycobacteria, especially M. tuberculosis complex organisms and other slow growing mycobacteria. The present invention provides a recombinant mycobacterium which expresses a DNA of interest incorporated into its chromosome by a TM4 conditional shuttle phasmid containing the DNA of interest. The present invention further provides a mycobacterial auxotrophic mutant and a method of generating auxotrophic mutants.

L3 ANSWER 12 OF 12 USPATFULL on STN
AN 1998:75416 USPATFULL
TI D29 shuttle phasmids and uses thereof
IN Jacobs, William R., City Island, NY, United States
Hatfull, Graham F., Pittsburgh, PA, United States
PA Albert Einstein College of Medicine of Yeshiva University, a Division of Yeshiva University, Bronx, NY, United States (U.S. corporation)
University of Pittsburgh, Pittsburgh, PA, United States (U.S. corporation)
PI US 5773267 19980630
AI US 1996-614770 19960307 (8)
RLI Continuation-in-part of Ser. No. US 1994-247901, filed on 23 May 1994 which is a continuation-in-part of Ser. No. US 1993-57531, filed on 29 Apr 1993, now abandoned which is a continuation-in-part of Ser. No. US 1992-833431, filed on 7 Feb 1992, now abandoned
DT Utility
FS Granted
EXNAM Primary Examiner: Degen, Nancy; Assistant Examiner: Schwartzman, Robert
LREP Amster, Rothstein & Ebenstein
CLMN Number of Claims: 15
ECL Exemplary Claim: 2
DRWN 2 Drawing Figure(s); 2 Drawing Page(s)
LN.CNT 906
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention provides a conditional shuttle phasmid constructed by inserting a cosmid into a non-essential region of the D29 mycobacteriophage which is capable of introducing DNA of interest into the chromosome of mycobacteria, especially M. tuberculosis complex organisms and other slow growing mycobacteria. The present invention provides a recombinant mycobacterium which expresses a DNA of interest incorporated into its chromosome by a conditional shuttle plasmid containing the DNA of interest. The present invention further provides a mycobacterial auxotrophic mutant and method of generating auxotrophic mutants. Finally, the present invention provides a method of inactivating a mycobacterial virulence gene.

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L5   ANSWER 1 OF 3  USPATFULL on STN
AN     2003:194142  USPATFULL
TI     D-alanine racemase mutants of mycobacteria and uses therefore
IN     Barletta, Raul G., Lincoln, NE, UNITED STATES
       Barletta-Chacon, Ofelia, Lincoln, NE, UNITED STATES
PI     US 2003133952       A1  20030717
       US 6929799          B2  20050816
AI     US 2002-323351      A1  20021218 (10)
PRAI   US 2001-341485P     20011218 (60)
DT     Utility
FS     APPLICATION
LN.CNT 1398
INCL   INCLM: 424/248.100
       INCLS: 514/423.000
NCL    NCLM:  424/248.100
       NCLS:  424/009.100; 424/009.200; 424/093.100; 424/093.200; 424/184.100;
              424/200.100; 424/234.100; 435/243.000; 435/252.100; 435/253.100;
              514/423.000
IC     [7]
       ICM    A61K039-04
       ICS    A61K031-4015
       IPCI   A61K0039-04 [ICM,7]; A61K0031-4015 [ICS,7]
       IPCI-2 A61K0039-04 [ICM,7]; A61K0039-02 [ICS,7]; C12N0001-00 [ICS,7]
       IPCR   A61K0039-04 [I,C*]; A61K0039-04 [I,A]
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L5   ANSWER 2 OF 3  USPATFULL on STN
AN     2002:126349  USPATFULL
TI     Identification of virulence determinants
IN     Barletta, Raul G., Lincoln, NE, UNITED STATES
       Harris, N. Beth, Lincoln, NE, UNITED STATES
PI     US 2002064861       A1  20020530
AI     US 2001-759287      A1  20010111 (9)
PRAI   US 2000-175433P     20000111 (60)
DT     Utility
FS     APPLICATION
LN.CNT 1276
INCL   INCLM: 435/252.300
NCL    NCLM:  435/252.300
IC     [7]
       ICM    C12N001-20
       IPCI   C12N0001-20 [ICM,7]
       IPCR   C12Q0001-04 [I,C*]; C12Q0001-04 [I,A]
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L5   ANSWER 3 OF 3  USPATFULL on STN
AN     2001:59388  USPATFULL
TI     Recombinant mycobacteria auxotrophic for diaminopimelate
IN     Pavelka, Jr., Martin S., Bronx, NY, United States
       Jacobs, Jr., William R., City Island, NY, United States
PA     Albert Einstein College of Medicine of Yeshiva University, Bronx, NY,
       United States (U.S. corporation)
PI     US 6221364          B1  20010424
AI     US 1996-747177          19961112 (8)
DT     Utility
FS     Granted
LN.CNT 1347
INCL   INCLM: 424/248.100
       INCLS: 424/234.100; 424/184.100; 424/200.100; 435/172.100; 435/252.100;
              435/253.100; 435/252.300; 435/091.400; 935/065.000
NCL    NCLM:  424/248.100
       NCLS:  424/184.100; 424/200.100; 424/234.100; 435/091.400; 435/252.100;
              435/252.300; 435/253.100; 435/471.000; 435/473.000; 435/476.000
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IC [7]
ICM A61K039-04
ICS C12N015-64; C12N001-12; C12N001-20
IPCI A61K0039-04 [ICM,7]; C12N0015-64 [ICS,7]; C12N0001-12 [ICS,7]; C12N0001-20 [ICS,7]
IPCR A61K0039-04 [I,A]; A61K0039-04 [I,C*]; C12N0015-74 [I,A]; C12N0015-74 [I,C*]
EXF 424/234.1; 424/184.1; 424/248.1; 424/200.1; 424/172.1; 435/91.4; 435/252.1; 435/253.1; 435/252.3; 935/65
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

=> d bib ab 1-
YOU HAVE REQUESTED DATA FROM 62 ANSWERS - CONTINUE? Y/(N):y

L5 ANSWER 1 OF 62 MEDLINE on STN
AN 2007115276 MEDLINE
DN PubMed ID: 17204371
TI Differential expression of NF-kappaB in mycobacteria infected THP-1 affects apoptosis.
AU Dhiman Rohan; Raje Manoj; Majumdar Sekhar
CS Division of Cell Biology and Immunology, Institute of Microbial Technology (CSIR), Chandigarh 160 036, India.
SO Biochimica et biophysica acta, (2007 Apr) Vol. 1770, No. 4, pp. 649-58. Electronic Publication: 2006-12-06. Journal code: 0217513. ISSN: 0006-3002.
CY Netherlands
DT Journal; Article; (JOURNAL ARTICLE) (RESEARCH SUPPORT, NON-U.S. GOV'T)
LA English
FS Priority Journals
EM 200704
ED Entered STN: 27 Feb 2007
Last Updated on STN: 18 Apr 2007
Entered Medline: 17 Apr 2007
AB The present study was conducted to see the role of NF-kappaB in virulent (Mycobacterium tuberculosis H37Rv) and avirulent (M. tuberculosis H37Ra) mycobacterial infection in THP-1 cells. To inactivate NF-kappaB, pCMV-IkappaBalphaM dn containing THP-1 cell line was generated which showed marked increase in apoptosis with M. tuberculosis H37Rv and M. tuberculosis H37Ra. Infected THP-1-IkappaBalphaM dn cells showed decrease in mitochondrial membrane potential, cytochrome c release, activation of caspase-3 and enhanced TNF-alpha production. Increase in apoptosis of infected THP-1-IkappaBalphaM dn cells resulted in inhibition of intracellular mycobacterial growth. Differential NF-kappaB activation potential was observed with M. tuberculosis H37Rv and M. tuberculosis H37Ra. Both the strains activated NF-kappaB after 4 h in THP-1 cells however after 48 h only M. tuberculosis H37Rv activated NF-kappaB which lead to up-regulation of bcl-2 family anti-apoptotic member, bfl-1/A1. Our results indicated that NF-kappaB activation may be a determinant factor for the success of virulent mycobacteria within macrophages.

L5 ANSWER 2 OF 62 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
DUPLICATE 1
AN 2007:218400 BIOSIS
DN PREV200700218117
TI Expression, production and release of the Eis protein by Mycobacterium tuberculosis during infection of macrophages and its effect on cytokine secretion.
AU Samuel, Linoj P. [Reprint Author]; Song, Chang-Hwa; Wei, Jun; Roberts, Esteban A.; Dahl, John L.; Barry, Clifton E. III; Jo, Eun-Kyeong; Friedman, Richard L.
CS Univ Rochester, Dept Clin Microbiol, 601 Elmwood Ave,Box 710, Rochester, NY 14642 USA
Linoj_Samuel@urmc.rochester.edu
SO Microbiology (Reading), (FEB 2007) Vol. 153, No. Part 2, pp. 529-540. ISSN: 1350-0872.
DT Article
LA English
ED Entered STN: 28 Mar 2007
Last Updated on STN: 28 Mar 2007
AB The eis gene of Mycobacterium tuberculosis has been shown to play a role in the survival of the avirulent Mycobacterium smegmatis within the macrophage. In vitro and in vivo analysis of Delta eis deletion mutants and complemented

strains showed no effect on survival of M. tuberculosis in U-937 macrophages or in a mouse aerosol infection model, respectively. Further studies were done in an attempt to determine the role of eis in M. tuberculosis intracellular survival and to define a phenotypic difference between wild-type and the Delta eis deletion mutant. Bioinformatic analysis indicated that Eis is an acetyltransferase of the GCN5-related family of N-acetyltransferases. Immunofluorescence microscopy and Western blot analysis studies demonstrated that Eis is released into the cytoplasm of M. tuberculosis-infected U-937 macrophages. Eis was also found in the extravesicular fraction and culture supernatant of M. tuberculosis-infected macrophages. The effect of Eis on human macrophage cytokine secretion was also examined. Eis modulated the secretion of IL-10 and TNF-alpha by primary human monocytes in response both to infection with M. tuberculosis and to stimulation with recombinant Eis protein. These results suggest that Eis is a mycobacterial effector that is released into the host cell to modulate inflammatory responses, possibly via transcriptional or post-translational means.

L5 ANSWER 3 OF 62 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
DUPLICATE 2
AN 2006:295676 BIOSIS
DN PREV200600292473
TI A mycobacterial operon essential for virulence in vivo and invasion and intracellular persistence in macrophages.
AU Gao, Lian-Yong [Reprint Author]; Pak, Melissa; Kish, Rabab; Kajihara, Kimberly; Brown, Eric J.
CS Univ Calif San Francisco, Program Microbial Pathogenesis and Host Def, 600 16th St,Campus Box 2140, San Francisco, CA 94143 USA lygao@umd.edu; ebrown@medicine.ucsf.edu
SO Infection and Immunity, (MAR 2006) Vol. 74, No. 3, pp. 1757-1767. CODEN: INFIBR. ISSN: 0019-9567.
DT Article
LA English
ED Entered STN: 31 May 2006
Last Updated on STN: 31 May 2006
AB The ability to invade and grow in macrophages is necessary for Mycobacterium tuberculosis to cause disease. We have found a Mycobacterium marinum locus of two genes that is required for both invasion and intracellular survival in macrophages. The genes were designated iipA (mycobacterial invasion and intracellular persistence) and iipB. The iip mutant, which was created by insertion of a kanamycin resistance gene cassette at the 5' region of iipA, was completely avirulent to zebra fish. Expression of the M. tuberculosis orthologue of iipA, Rv1477, fully complemented the iip mutant for infectivity in vivo, as well as for invasion and intracellular persistence in macrophages. In contrast, the iipB orthologue, Rv1478, only partially complemented the iip mutant in vivo and restored invasion but not intracellular growth in macrophages. While IipA and lipB differ at their N termini, they are highly similar throughout their C-terminal NLPC_p60 domains. The p60 domain of Rv1478 is fully functional to replace that of Rv1477, suggesting that the N-terminal sequence of Rv1477 is required for full virulence in vivo and in macrophages. Further mutations demonstrated that both Arg-Gly-Asp (RGD) and Asp-Cys-Ser-Gly (DCSG) sequences in the p60 domain are required for function. The iip mutant exhibited increased susceptibility to antibiotics and lysozyme and failed to fully separate daughter cells in liquid culture, suggesting a role for iip genes in cell wall structure and function. Altogether, these studies demonstrate an essential role for a p60-containing protein, IipA, in the pathogenesis of M. marinum infection.

L5 ANSWER 4 OF 62 MEDLINE on STN
AN 2006329001 MEDLINE
DN PubMed ID: 16710161

TI [Mendelian susceptibility to mycobacterial disease: defects in the IL-12/IFNgamma pathway].
Susceptibilite mendelienne aux infections mycobacteriennes: defauts de l'axe IL-12/IFNgamma.
AU Fieschi Claire
CS Departement d'immunologie, Unite d'immunopathologie, Hopital Saint-Louis, AP-HP, Paris (75).. claire.fieschi@sls.aphp.fr
SO Presse medicale (Paris, France : 1983), (2006 May) Vol. 35, No. 5 Pt 2, pp. 879-86. Ref: 27
Journal code: 8302490. ISSN: 0755-4982.
CY France
DT (ENGLISH ABSTRACT)
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LA French
FS Priority Journals
EM 200606
ED Entered STN: 6 Jun 2006
Last Updated on STN: 23 Jun 2006
Entered Medline: 22 Jun 2006
AB Mendelian susceptibility to mycobacterial disease is a recently described entity, responsible for disseminated disease due to nonvirulent mycobacteria and, to a lesser extent, non-typhoid salmonella in otherwise healthy patients. Different mutations in 5 genes and allelic heterogeneity accounts for 12 different diseases. The proteins encoded by the mutated alleles all belong to the interferon gamma/interleukin 12 loop, a hallmark of granulomatous immune response. Patients with defects in the IFNgamma pathway are predisposed to mycobacterial diseases, while those with defects in the IL-12 pathway are threatened more often by non-typhoid (systemic) salmonellosis. Tuberculosis has been described in both of these signaling pathway defects. Genetic dissection of the IL-12/IFNgamma pathway should improve our understanding of the human immune response to mycobacteria and help us begin to elucidate the genetic bases of tuberculosis.

L5 ANSWER 5 OF 62 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN DUPLICATE 3
AN 2006:269142 BIOSIS
DN PREV200600267374
TI Neutral-red reaction is related to virulence and cell wall methyl-branched lipids in Mycobacterium tuberculosis.
AU Cardona, P.-J.; Soto, C. Y.; Martin, C.; Giquel, B.; Agusti, G.; Guirado, E.; Sirakova, T.; Kolattukudy, P.; Julian, E.; Luquin, M. [Reprint Author]
CS Univ Autonoma Barcelona, Fac Ciencies, Dept Genet and Microbiol, E-08193 Barcelona, Spain
marina.luquin@uab.es
SO Microbes and Infection, (JAN 2006) Vol. 8, No. 1, pp. 183-190.
ISSN: 1286-4579.
DT Article
LA English
ED Entered STN: 10 May 2006
Last Updated on STN: 10 May 2006
AB Searching for virulence marking tests for Mycobacteritan tuberculosis, Dubos and Middlebrook reported in 1948 that in an alkaline aqueous solution of neutral-red, the cells of the virulent H37Rv M. tuberculosis strain fixed the dye and became red in color, whereas the cells of the avirulent H37Ra M. tuberculosis strain remained unstained. In the 1950 and 1960s, fresh isolates of M. tuberculosis were tested for this neutral-red cytochemical reaction and it was reported that they were neutral-red positive, whereas other mycobacteria of diverse environmental origins that were non-pathogenic for guinea pigs were neutral-red negative. However, neutral-red has not really been proven to be a virulence marker. To test if virulence is in fact

correlated to neutral-red, we studied a clinical isolate of M. tuberculosis that was originally neutral-red positive but, after more than I year passing through culture mediums, turned neutral-red negative. We found that, in comparison to the original neutral-red positive strain, this neutral-red negative variant was attenuated in two murine models of experimental tuberculosis. Lipid analysis showed that this neutral-red negative natural mutant lost the capacity to synthesize pthiocerol dimycocerosates, a cell wall methyl-branched lipid that has been related to virulence in M. tuberculosis. We also studied the neutral-red of different gene-targeted M. tuberculosis mutants unable to produce pthiocerol dimycocerosates or other cell wall methyl-branched lipids such as sulfolipids, and polyacyltrehaloses. We found a negative neutral-red reaction in mutants that were deficient in more than one type of methyl-branched lipids. We conclude that neutral-red is indeed a marker of virulence and it indicates important perturbations in the external surface of M. tuberculosis cells.

L5 ANSWER 6 OF 62 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2005:1346174 CAPLUS
DN 144:81971
TI Inactivation of pyridoxal 5'-phosphate biosynthesis genes pdx in construction of avirulent strains of pathogens for vaccine use
IN Belitsky, Boris R.
PA USA
SO U.S. Pat. Appl. Publ., 23 pp.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 2005287169	A1	20051229	US 2004-869322	20040616
PRAI US 2003-479331P	P	20030617		

AB A method of attenuating a bacterial pathogen by an inactivating mutation in a pdx gene for pyridoxal 5'-phosphate biosynthesis is described. These attenuated strains are auxotrophic for pyridoxal phosphate and can be used in vaccines and to screen for antibacterial compds. Thus, Bacillus subtilis genes yaaD and yaaE were shown to be homologs of pdxS and pdxT genes involved in pyridoxal 5'-phosphate biosynthesis. The two genes form an operon. PdxS and PdxT formed a complex with glutaminase activity. No revertants or pseudorevertants of pdxS, or pdxST, null mutants were observed Another gene, called pdxZ, was identified as a novel type of pyridoxal kinase involved in the salvage pathway of pyridoxal 5'-phosphate biosynthesis. Double pdxS-pdxZ mutants were only able to grow when the culture medium was supplemented with very high concns. of pyridoxal.

L5 ANSWER 7 OF 62 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
DUPLICATE 4
AN 2005:226576 BIOSIS
DN PREV200510014058
TI Transposon mutagenesis of Mb0100 at the ppe1-nrp locus in Mycobacterium bovis disrupts phthiocerol dimycocerosate (PDIM) and glycosylphenol-PDIM biosynthesis, producing an avirulent strain with vaccine properties at least equal to those of M-bovis BCG.
AU Hotter, Grant S. [Reprint Author]; Wards, Barry J.; Mouat, Pania; Besra, Gurdyal S.; Gomes, Jessica; Singh, Monica; Bassett, Shalome; Kawakami, Pamela; Wheeler, Paul R.; de Lisle, Geoffrey W.; Collins, Desmond M.
CS Wallaceville Anim Res Ctr, AgRes, POB 40063, Upper Hutt, New Zealand
grant.hotter@agresearch.co.nz
SO Journal of Bacteriology, (APR 2005) Vol. 187, No. 7, pp. 2267-2277.
CODEN: JOBAAY. ISSN: 0021-9193.
DT Article

LA English
ED Entered STN: 16 Jun 2005
Last Updated on STN: 16 Jun 2005
AB The unusual and complex cell wall of pathogenic mycobacteria plays a major role in pathogenesis, with specific complex lipids acting as defensive, offensive, or adaptive effectors of virulence. The phthiocerol and phthiodiolone dimycocerosate esters (PDIMs) comprise one such category of virulence-enhancing lipids. Recent work in several laboratories has established that the Mycobacterium tuberculosis fadD26-mmpL7 (Rv2930-Rv2942) locus plays a major role in PDIM biosynthesis and secretion and that PDIM is required for virulence. Here we describe two independent transposon mutants (WAg533 and WAg537) of Mycobacterium bovis, both of which carry an insertion in Mb0100 (= M. tuberculosis Rv0097) to reveal a new locus involved in PDIM biosynthesis. The mutations have a polar effect on expression of the downstream genes Mb0101, Mb0102 (fadD10), Mb0103, and Mb0104 (nrp), and Mb0100 is shown to be in an operon comprising these genes and Mb0099. Reverse transcription-PCR analysis shows elevated transcription of genes in the operon upstream from the transposon insertion sites in both mutants. Both mutants have altered colony morphology and do not synthesize PDIMs or glycosylphenol-PDIM. Both mutants are avirulent in a guinea pig model of tuberculosis, and when tested as a vaccine, WAg533 conferred protective immunity against M. bovis infection at least equal to that afforded by M. bovis bacillus Calmette-Guerin.

L5 ANSWER 8 OF 62 MEDLINE on STN
AN 2005034739 MEDLINE
DN PubMed ID: 15661908
TI Elemental analysis of Mycobacterium avium-, Mycobacterium tuberculosis-, and Mycobacterium smegmatis-containing phagosomes indicates pathogen-induced microenvironments within the host cell's endosomal system.
AU Wagner Dirk; Maser Jorg; Lai Barry; Cai Zhonghou; Barry Clifton E 3rd; Honer Zu Bentrup Kerstin; Russell David G; Bermudez Luiz E
CS Kuzell Institute for Arthritis and Infectious Diseases, San Francisco, CA 94115, USA.
NC R01-AI 47010 (NIAID)
SO Journal of immunology (Baltimore, Md. : 1950), (2005 Feb 1) Vol. 174, No. 3, pp. 1491-500.
Journal code: 2985117R. ISSN: 0022-1767.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
(RESEARCH SUPPORT, U.S. GOV'T, NON-P.H.S.)
(RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 200503
ED Entered STN: 25 Jan 2005
Last Updated on STN: 16 Mar 2005
Entered Medline: 15 Mar 2005
AB Mycobacterium avium and Mycobacterium tuberculosis are human pathogens that infect and replicate within macrophages. Both organisms live in phagosomes that fail to fuse with lysosomes and have adapted their lifestyle to accommodate the changing environment within the endosomal system. Among the many environmental factors that could influence expression of bacterial genes are the concentrations of single elements within the phagosomes. We used a novel hard x-ray microprobe with suboptical spatial resolution to analyze characteristic x-ray fluorescence of 10 single elements inside phagosomes of macrophages infected with M. tuberculosis and M. avium or with avirulent M. smegmatis. The iron concentration decreased over time in phagosomes of macrophages infected with Mycobacterium smegmatis but increased

in those infected with pathogenic mycobacteria. Autoradiography of infected macrophages incubated with (59)Fe-loaded transferrin demonstrated that the bacteria could acquire iron delivered via the endocytic route, confirming the results obtained in the x-ray microscopy. In addition, the concentrations of chlorine, calcium, potassium, manganese, copper, and zinc were shown to differ between the vacuole of pathogenic mycobacteria and M. smegmatis. Differences in the concentration of several elements between M. avium and M. tuberculosis vacuoles were also observed. Activation of macrophages with recombinant IFN-gamma or TNF-alpha before infection altered the concentrations of elements in the phagosome, which was not observed in cells activated following infection. Siderophore knockout M. tuberculosis vacuoles exhibited retarded acquisition of iron compared with phagosomes with wild-type M. tuberculosis. This is a unique approach to define the environmental conditions within the pathogen-containing compartment.

L5 ANSWER 9 OF 62 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
DUPLICATE 5
AN 2005:453443 BIOSIS
DN PREV200510234175
TI Mycobacterium ulcerans toxic macrolide, mycolactone modulates the host immune response and cellular location of M-ulcerans in vitro and in vivo.
AU Adusumilli, Sarojini; Mve-Obiang, Armand; Sparer, Tim; Meyers, Wayne; Hayman, John; Small, Pamela Long Claus [Reprint Author]
CS Univ Tennessee, Dept Microbiol, Knoxville, TN 37996 USA
psmall@utk.edu
SO Cellular Microbiology, (SEP 2005) Vol. 7, No. 9, pp. 1295-1304.
ISSN: 1462-5814.
DT Article
LA English
ED Entered STN: 3 Nov 2005
Last Updated on STN: 3 Nov 2005
AB Mycobacterium ulcerans produces an extracellular cutaneous infection (Buruli ulcer) characterized by immunosuppression. This is in stark contrast to all other pathogenic Mycobacteria species that cause intracellular, granulomatous infections. The unique mycobacterial pathology of M. ulcerans infection is attributed to a plasmid-encoded immunomodulatory macrolide toxin, mycolactone. In this article we explore the role of mycolactone in the virulence of M. ulcerans using mycolactone and genetically defined mycolactone negative mutants. In a guinea pig infection model wild-type (WT) M. ulcerans produces an extracellular infection whereas mycolactone negative mutants produce an intracellular inflammatory infection similar to that of Mycobacterium marinum. Although mycolactone negative mutants are avirulent, they persist for at least 6 weeks. Chemical complementation of M. ulcerans mutants with mycolactone restores WT M. ulcerans pathology. Mycolactone negative mutants are capable of growth within macrophages in vitro whereas macrophages are killed by WT M. ulcerans. The ability of mycolactone to caused delayed cell death via apoptosis has been reported. However, mycolactone also causes cell death via necrosis. In vitro mycolactone has antiphagocytic properties. Neither WT M. ulcerans nor mycolactone negative strains are strong neutrophil attractants. These results suggest that mycolactone is largely responsible for the unique pathology produced by M. ulcerans.

L5 ANSWER 10 OF 62 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2006:621162 CAPLUS
DN 146:199474
TI Identification of differential genomic genes between Mycobacterium tuberculosis H37Rv and H37Ra strains by differential display
AU Xiong, Zhihong; Zhuang, Yuhui; Li, Guoli
CS Tuberculosis Research Laboratory, The 309th Hospital of PLA, Beijing,

100091, Peop. Rep. China
SO Weishengwuxue Tongbao (2005), 32(3), 57-61
CODEN: WSWPDI; ISSN: 0253-2654
PB Kexue Chubanshe
DT Journal
LA Chinese
AB Differential display (DD)-PCR was used to clone the differential expressed genes between Mycobacterium tuberculosis virulent strain H37Rv and its avirulent mutant H37Ra. All of different genes were cloned, sequenced, and some were analyzed by Northern blotting. Two cDNAs that express in H37Rv but not in H37Ra were cloned and sequenced, Rv0170 and Rv1894c, code for proteins with unknown functions. The two genes were present in H37Ra, but not expressed. These results showed that mRNA DD methodol. can represent a potential tool for research on M. tuberculosis gene expression.

L5 ANSWER 11 OF 62 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2004:80234 CAPLUS
DN 140:144687
TI Molecular differences between species of the Mycobacterium tuberculosis complex by genetic deletion markers and genetic marker-encoded antigens
IN Behr, Marcel; Small, Peter; Wilson, Michael A.; Schoolnik, Gary; Aagaard, Claus; Rosenkrands, Ida; Weldingh, Karin; Andersen, Peter
PA Can.
SO U.S. Pat. Appl. Publ., 83 pp., Cont.-in-part of U.S. Ser. No. 894,844.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2004018574	A1	20040129	US 2003-388902	20030314
	US 6291190	B1	20010918	US 1999-318191	19990525
	US 2002176873	A1	20021128	US 2001-894844	20010627
	US 6686166	B2	20040203		
	US 2004063923	A1	20040401	US 2003-647089	20030821
	WO 2004083448	A2	20040930	WO 2004-US7668	20040311
	WO 2004083448	A3	20060216		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	US 2006002953	A1	20060105	US 2005-143401	20050601
	IN 2005CN02249	A	20070406	IN 2005-CN2249	20050913
PRAI	US 1998-97936P	P	19980825		
	US 1999-318191	A1	19990525		
	US 2001-894844	A2	20010627		
	US 2003-388902	A	20030314		
	US 2003-647089	B1	20030821		
	WO 2004-US7668	W	20040311		

AB Specific genetic deletions are identified that serve as markers to distinguish between avirulent and virulent mycobacteria strains, including M. bovis, M. bovis BCG strains, M. tuberculosis (M. tb.) isolates, and bacteriophages that infect mycobacteria. These deletions are used as genetic markers to distinguish between the different mycobacteria. In one embodiment of the invention, a

plurality of antigens encoded by the provided genetic markers is used in the diagnosis of M. tuberculosis infection. Alternatively, the deleted genes are identified in the M. tb. genome sequence, and are then reintroduced by recombinant methods into BCG or other vaccine strains, in order to improve the efficacy of vaccination.

L5 ANSWER 12 OF 62 MEDLINE on STN
AN 2004235519 MEDLINE
DN PubMed ID: 15121875
TI Acquisition of Hrs, an essential component of phagosomal maturation, is impaired by mycobacteria.
AU Vieira Otilia V; Harrison Rene E; Scott Cameron C; Stenmark Harald; Alexander David; Liu Jun; Gruenberg Jean; Schreiber Alan D; Grinstein Sergio
CS Cell Biology Program, Hospital for Sick Children, and Department of Biochemistry, University of Toronto, Ontario M5G 1X8, Canada.
SO Molecular and cellular biology, (2004 May) Vol. 24, No. 10, pp. 4593-604. Journal code: 8109087. ISSN: 0270-7306.
CY United States
DT Journal; Article; (JOURNAL ARTICLE) (RESEARCH SUPPORT, NON-U.S. GOV'T)
LA English
FS Priority Journals
EM 200406
ED Entered STN: 12 May 2004
Last Updated on STN: 18 Jun 2004
Entered Medline: 17 Jun 2004
AB Pathogenic mycobacteria survive within macrophages by precluding the fusion of phagosomes with late endosomes or lysosomes. Because the molecular determinants of normal phagolysosome formation are poorly understood, the sites targeted by mycobacteria remain unidentified. We found that Hrs, an adaptor molecule involved in protein sorting, associates with phagosomes prior to their fusion with late endosomes or lysosomes. Recruitment of Hrs required the interaction of its FYVE domain with phagosomal phosphatidylinositol 3-phosphate, but two other attachment sites were additionally involved. Depletion of Hrs by use of small interfering RNA impaired phagosomal maturation, preventing the acquisition of lysobisphosphatidic acid and reducing luminal acidification. As a result, the maturation of phagosomes formed in Hrs-depleted cells was arrested at an early stage, characterized by the acquisition and retention of sorting endosomal markers. This phenotype is strikingly similar to that reported to occur in phagosomes of cells infected by mycobacteria. We therefore tested whether Hrs is recruited to phagosomes containing mycobacteria. Hrs associated readily with phagosomes containing inert particles but poorly with mycobacterial phagosomes. Moreover, Hrs was found more frequently in phagosomes containing avirulent Mycobacterium smegmatis than in phagosomes with the more virulent Mycobacterium marinum. These findings suggest that the inability to recruit Hrs contributes to the arrest of phagosomal maturation induced by pathogenic mycobacteria.

L5 ANSWER 13 OF 62 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN DUPLICATE 6
AN 2004:135078 BIOSIS
DN PREV200400138523
TI A two-component signal transduction system with a PAS domain-containing sensor is required for virulence of Mycobacterium tuberculosis in mice.
AU Rickman, Lisa; Saldanha, Jose W.; Hunt, Debbie M.; Hoar, Dominic N.; Colston, M. Joseph; Millar, Jonathan B. A.; Buxton, Roger S. [Reprint Author]
CS Division of Mycobacterial Research, National Institute for Medical Research, Mill Hill, London, NW7 1AA, UK

lr2@sanger.ac.uk; jsaldan@nimr.mrc.ac.uk; dhunt@nimr.mrc.ac.uk; dhoar@nimr.mrc.ac.uk; jmillar@nimr.mrc.ac.uk; rbuxton@nimr.mrc.ac.uk

SO Biochemical and Biophysical Research Communications, (January 30 2004) Vol. 314, No. 1, pp. 259-267. print.
CODEN: BBRCA9. ISSN: 0006-291X.

DT Article

LA English

ED Entered STN: 10 Mar 2004
Last Updated on STN: 10 Mar 2004

AB Mycobacterium tuberculosis, the causative organism of tuberculosis, encounters oxidative stress during phagocytosis by the macrophage and following macrophage activation during an acquired immune response, and also from internally generated sources of radical oxygen intermediates through intermediary metabolism. We have identified the SenX3 protein, a sensor in 1 of the 11 complete pairs of two-component signal transduction systems in M. tuberculosis, as a possible orthologue of the Mak2p protein from the fission yeast Schizosaccharomyces pombe that is known to sense peroxide stress. Moreover, the SenX3-RegX3 two-component system was the top scoring hit in a homology search with the Escherichia coli ArcB-ArcA global control system of aerobic genes. Using structural modelling techniques we have determined that SenX3 contains a PAS-like domain found in a variety of prokaryotic and eukaryotic sensors of oxygen and redox. Mutants with knock-outs of senX3 or of the accompanying transcriptional regulator regX3 were constructed and found to have reduced virulence in a mouse model of tuberculosis infection, the mutant bacteria persisting for up to 4 months post-infection; complemented mutants had regained virulence confirming that it was mutations of this two-component system that were responsible for the avirulent phenotype. This work identifies the PAS domain as a possible drug target for tuberculosis and mutations in the senX3-regX signal transduction system as potentially useful components of live vaccine strains.

L5 ANSWER 14 OF 62 CAPLUS COPYRIGHT 2007 ACS on STN

AN 2004:232187 CAPLUS

DN 140:405118

TI The interleukin-12/interferon-γ loop is required for protective immunity to experimental and natural infections by Mycobacterium

AU Bonnet, Marion; Soudais, Claire; Casanova, Jean-Laurent

CS Laboratory of Human Genetics of Infectious Diseases, Necker Medical School, Universite Rene Descartes, Paris, Fr.

SO Advances in Molecular and Cellular Microbiology (2004), 4(Susceptibility to Infectious Diseases), 259-278
CODEN: AMCMDX

PB Cambridge University Press

DT Journal; General Review

LA English

AB A review. Mendelian susceptibility to poorly pathogenic mycobacteria, such as bacillus Calmette-Guerin (BCG) and environmental nontuberculous mycobacteria (EM), is a rare human syndrome. Some patients present with mutations in the genes encoding IL-12p40 or IL12Rβ1, associated with impaired production of IFNγ. Others carry mutations in the genes encoding IFNγR1, IFNγR2, or STAT1, associated with impaired response to IFNγ. Knockout mice for IL-12, IFNγ, or their receptors are also vulnerable to exptl. infection with nonvirulent mycobacteria. Studies with knockout mice also implicate other mols. involved in the induction of, or response to, IFNγ, such as IL-18, IL-1, TNFα, IRF-1, and NOS2, in the control of mycobacterial infection. It is now clear that the IL-12-IFNγ loop is crucial for protective immunity to exptl. and natural mycobacterial infection in both mice and men.

RE.CNT 81 THERE ARE 81 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 15 OF 62 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN DUPLICATE 7
AN 2004:352407 BIOSIS
DN PREV200400352974
TI The Mycobacterium tuberculosis complex transcriptome of attenuation.
AU Mostowy, Serge; Cleto, Cynthia; Sherman, David R.; Behr, Marcel A. [Reprint Author]
CS Div Infect Dis and Med Microbiol, Montreal Gen Hosp, 1650 Cedar Ave,A5-156, Montreal, PQ, H3G 1A4, Canada
marcel.behr@mcgill.ca
SO Tuberculosis (Amsterdam), (2004) Vol. 84, No. 3-4, pp. 197-204. print.
ISSN: 1472-9792 (ISSN print).
DT Article
LA English
ED Entered STN: 26 Aug 2004
Last Updated on STN: 26 Aug 2004
AB Although the deletion of RD1 is likely correlated to attenuation from virulence for members of the Mycobacterium tuberculosis (MTB) complex, the reasons for this phenotype remain to be fully explained. As genomic variation is responsible for at least a component of variability in gene expression, we Looked to the in vitro global expression profile of the RD1 artificial. knockout from M. tuberculosis H37Rv (H37Rv:DELTARD1) for clues to elucidate its phenotypic shift towards attenuation. By comparing the transcriptome of H37Rv:DELTARD1 to that of virulent H37Rv, 15 regulated genes located in nine different regions outside of RD1 have been identified, capturing an effect of RD1's deletion on the rest of the genome. To assess whether these regulations are characteristic of attenuated MTB in general, expression profiles of natural RD1 mutants (BCG Russia, BCG Pasteur, and M. microti) as well as the ' avirulent' M. tuberculosis H37Ra, whose RD1 region is genomically intact, were obtained. Results indicate that attenuated strains lack the expression of RD1 genes including cfp10 and esat6, whether through deletion or reduced expression. Furthermore, comparative transcriptomics reveals the concurrent down-regulation of several gene neighborhoods beyond RD1. The potential relevance of these other expression changes towards MTB virulence is discussed. Copyright 2004 Elsevier Ltd. ALL rights reserved.

L5 ANSWER 16 OF 62 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2003:1007913 CAPLUS
DN 140:54533
TI Sequences of virulence genes of M. marinum and M. tuberculosis and use for preparing attenuated vaccines
IN Trucksis, Michele
PA United States of America Dept. of Veterans Affairs, USA; University of Maryland
SO U.S. Pat. Appl. Publ., 65 pp.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 2

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 2003236393	A1	20031225	US 2003-394575	20030324
WO 2001019993	A2	20010322	WO 2000-US25512	20000918
WO 2001019993	A3	20011122		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRAI WO 2000-US25512 A 20000918
US 2002-366262P P 20020322
US 2002-367206P P 20020326
US 1999-154322P P 19990917

AB The present invention provides methods for identifying, isolating and mutagenizing virulence genes of mycobacteria, e.g., M. marinum and M. tuberculosis. Also described are isolated virulence genes and fragments of them, isolated gene products and fragments of them, avirulent bacteria in which one or more virulence genes are mutagenized, attenuated vaccines containing such mutant bacteria, and methods to elicit an immune response in a host, using such mutant bacteria.

L5 ANSWER 17 OF 62 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2003:757013 CAPLUS
DN 139:272067
TI Mycobacterial sulfation pathway proteins and methods of use in drug screening
IN Bertozzi, Carolyn R.; Williams, Spencer J.; Mougous, Joseph D.
PA The Regents of The University of California, USA
SO U.S. Pat. Appl. Publ., 101 pp., Cont.-in-part of U.S. Ser. No. 126,279.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2003180321	A1	20030925	US 2002-286606	20021031
	US 6863895	B2	20050308		
	US 2003104001	A1	20030605	US 2002-126279	20020419
	US 6858213	B2	20050222		
	US 2004249131	A1	20041209	US 2004-891383	20040713
	US 6974580	B2	20051213		
	US 2006188517	A1	20060824	US 2005-218976	20050901
PRAI	US 2001-285394P	P	20010420		
	US 2001-345953P	P	20011026		
	US 2002-126279	A2	20020419		
	US 2002-286606	A3	20021031		
	US 2004-891383	A3	20040713		

AB Novel mycobacterial sulfation pathway proteins and polypeptides related thereto, as well as nucleic acid compns. encoding the same, are provided. The subject polypeptide and nucleic acid compns. find use in a variety of applications, including research, diagnostic, and therapeutic agent screening applications. Also provided are methods of inhibiting growth and/or virulence of a pathogenic mycobacterium, and methods of treating disease conditions associated with a pathogenic mycobacterium, particularly by administering an inhibitor of a mycobacterial sulfation pathway protein. The present invention further provides genetically modified mycobacteria having a defect in a sulfation pathway enzyme gene; and immunogenic compns. that include such genetically modified mycobacteria.

RE.CNT 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 18 OF 62 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN DUPLICATE 8
AN 2003:427090 BIOSIS
DN PREV200300427090
TI Glutamine synthetase GlnA1 is essential for growth of Mycobacterium tuberculosis in human THP-1 macrophages and guinea pigs.

AU Tullius, Michael V.; Harth, Gunter; Horwitz, Marcus A. [Reprint Author]
CS Division of Infectious Diseases, Department of Medicine, School of Medicine, UCLA, 10833 Le Conte Ave., CHS 37-121, Los Angeles, CA, 90095-1688, USA
mhorwitz@mednet.ucla.edu
SO Infection and Immunity, (July 2003) Vol. 71, No. 7, pp. 3927-3936. print.
ISSN: 0019-9567 (ISSN print).
DT Article
LA English
ED Entered STN: 17 Sep 2003
Last Updated on STN: 17 Sep 2003
AB To assess the role of glutamine synthetase (GS), an enzyme of central importance in nitrogen metabolism, in the pathogenicity of Mycobacterium tuberculosis, we constructed a glnA1 mutant via allelic exchange. The mutant had no detectable GS protein or GS activity and was auxotrophic for L-glutamine. In addition, the mutant was attenuated for intracellular growth in human THP-1 macrophages and avirulent in the highly susceptible guinea pig model of pulmonary tuberculosis. Based on growth rates of the mutant in the presence of various concentrations of L-glutamine, the effective concentration of L-glutamine in the M. tuberculosis phagosome of THP-1 cells was apprx10% of the level assayed in the cytoplasm of these cells (4.5 mM), indicating that the M. tuberculosis phagosome is impermeable to even very small molecules in the macrophage cytoplasm. When complemented by the M. tuberculosis glnA1 gene, the mutant exhibited a wild-type phenotype in broth culture and in human macrophages, and it was virulent in guinea pigs. When complemented by the Salmonella enterica serovar Typhimurium glnA gene, the mutant had only 1% of the GS activity of the M. tuberculosis wild-type strain because of poor expression of the S. enterica serovar Typhimurium GS in the heterologous M. tuberculosis host. Nevertheless, the strain complemented with S. enterica serovar Typhimurium GS grew as well as the wild-type strain in broth culture and in human macrophages. This strain was virulent in guinea pigs, although somewhat less so than the wild-type. These studies demonstrate that glnA1 is essential for M. tuberculosis virulence.

L5 ANSWER 19 OF 62 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN DUPLICATE 9
AN 2004:64114 BIOSIS
DN PREV200400065349
TI Different susceptibility of two animal species infected with isogenic mutants of Mycobacterium bovis identifies phoT as having roles in tuberculosis virulence and phosphate transport.
AU Collins, Desmond M. [Reprint Author]; Kawakami, R. Pamela; Buddle, Bryce M.; Wards, Barry J.; de Lisle, Geoffrey W.
CS Wallaceville Animal Research Centre, AgResearch, PO Box 40063, Upper Hutt, New Zealand
desmond.collins@agresearch.co.nz
SO Microbiology (Reading), (November 2003) Vol. 149, No. 11, pp. 3203-3212. print.
ISSN: 1350-0872 (ISSN print).
DT Article
LA English
ED Entered STN: 28 Jan 2004
Last Updated on STN: 28 Jan 2004
AB The Mycobacterium tuberculosis complex includes Mycobacterium bovis, which causes tuberculosis in most mammals, including humans. In previous work, it was shown that M. bovis ATCC 35721 has a mutation in its principal sigma factor gene, sigA, causing a single amino acid change affecting binding of SigA with the accessory transcription factor WhiB3. ATCC 35721 is avirulent when inoculated subcutaneously into guinea pigs but can be restored to virulence by integration of wild-type sigA to produce M. bovis WAg320.

Subsequently, it was surprising to discover that WAg320 was not virulent when inoculated intratracheally into the Australian brushtail possum (Trichosurus vulpecula), a marsupial that is normally very susceptible to infection with M. bovis. In this study, an in vivo complementation approach was used with ATCC 35721 to produce M. bovis WAg322, which was virulent in possums, and to identify the virulence-restoring gene, phoT. There are two point deletions in the phoT gene of ATCC 35721 causing frameshift inactivation, one of which is also in the phoT of BCG. Knockout of phoT from ATCC 35723, a virulent strain of M. bovis, produced M. bovis WAg758, which was avirulent in both guinea pigs and possums, confirming that phoT is a virulence gene. The effect on virulence of mode of infection versus animal species susceptibility was investigated by inoculating all the above strains by aerosol into guinea pigs and mice and comparing these to the earlier results. Characterization of PhoT indicated that it plays a role in phosphate uptake at low phosphate concentrations. At least in vitro, this role requires the presence of a wild-type sigA gene and appears separate from the ability of phoT to restore virulence to ATCC 35721. This study shows the advantages of using different animal models as tools for the molecular biological investigation of tuberculosis virulence.

L5 ANSWER 20 OF 62 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN DUPLICATE 10
AN 2004:103744 BIOSIS
DN PREV200400100041
TI Vaccine and skin testing properties of two avirulent Mycobacterium bovis mutants with and without an additional esat-6 mutation.
AU Collins, D. M. [Reprint Author]; Kawakami, R. P.; Wards, B. J.; Campbell, S.; De Lisle, G. W.
CS Wallaceville Animal Research Centre, AgResearch, P.O. Box 40063, Upper Hutt, New Zealand
desmond.collins@agresearch.co.nz
SO Tuberculosis (Amsterdam), (2003) Vol. 83, No. 6, pp. 361-366. print.
ISSN: 1472-9792 (ISSN print).
DT Article
LA English
ED Entered STN: 18 Feb 2004
Last Updated on STN: 18 Feb 2004
AB Setting: Molecular techniques are now available to develop new live tuberculosis vaccines by producing avirulent strains of the Mycobacterium tuberculosis complex with known genes deleted. Objectives: Determine if removal of esat-6 from new live tuberculosis vaccines with known attenuating mutations affects their vaccine efficacy and if it could enable the development of discriminating diagnostic tests. Design: Remove the esat-6 gene by allelic exchange from two illegitimate mutants of Mycobacterium bovis that had previously been shown to have similar vaccine efficacy to BCG in a guinea pig vaccination model. Determine the effect this removal has on virulence, vaccine efficacy and skin test reactivity in guinea pigs. Results: Two double knockout strains of M. bovis were produced and their virulence and vaccine efficacy were compared to their parent strains. Removal of the esat-6 gene had no significant effect on vaccine efficacy. In skin tests, animals inoculated with the double knockout strains reacted to PPD but not ESAT-6, whereas those inoculated with the parent strains had similar skin test reactivity to both PPD and esat-6. Conclusion: Removal of esat-6 from new live tuberculosis vaccine candidates has no significant effect on vaccine properties but does enable the use of skin tests to distinguish between vaccination and infection.

L5 ANSWER 21 OF 62 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
AN 2003:574190 BIOSIS
DN PREV200300577035

TI An avirulent, morphological mutant of Mycobacterium bovis with altered cell wall lipid biosynthesis.
AU Hotter, G. S. [Reprint Author]; Singh, M. [Reprint Author]; Campbell, S. [Reprint Author]; Wheeler, P. R.; De Lisle, G. W. [Reprint Author]; Collins, D. M. [Reprint Author]; Wards, B. J. [Reprint Author]
CS AgResearch, Upper Hutt, New Zealand
SO Abstracts of the General Meeting of the American Society for Microbiology, (2003) Vol. 103, pp. U-013. http://www.asmusa.org/mtgsrc/generalmeeting.htm. cd-rom.
Meeting Info.: 103rd American Society for Microbiology General Meeting. Washington, DC, USA. May 18-22, 2003. American Society for Microbiology. ISSN: 1060-2011 (ISSN print).
DT Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LA English
ED Entered STN: 10 Dec 2003
Last Updated on STN: 10 Dec 2003
AB Members of the Mycobacterium tuberculosis complex kill over two million people each year and a better vaccine is urgently needed. Mycobacterium bovis, a broad host range member of the complex, is probably responsible for up to 5% of these deaths and is also of major importance as a pathogen of domestic and wild animals. In the course of developing attenuated strains of M. bovis with efficacy as animal vaccines, we carried out transposon mutagenesis of the virulent M. bovis strain, WAg200, and identified a colony morphology mutant , WAg533. The mutant was avirulent in guinea pigs, and in vaccine trials provided protection at least equivalent to BCG. The transposon insertion site was found to disrupt the M. bovis gene equivalent to M. tuberculosis Rv0097. Reverse transcriptase PCR (rtPCR), using primer pairs spanning adjacent genes, demonstrated that Rv0097 is in an operon including Rv0096, Rv0097, and Rv0098. Disruption of Rv0097 had a polar effect on expression of Rv0098. Semi-quantitative rtPCR showed that expression of the operon was up-regulated in WAg533, indicating the possible operation of a feedback regulatory system. The altered colony morphology of WAg533 compared to WAg200 suggested that the mutation carried by WAg533 may affect cell wall biosynthesis. Given the importance of mycobacterial cell wall lipids in virulence and that altered lipid biosynthesis can affect colony morphology, we compared the polar and non-polar lipid profiles of WAg533 and WAg200 by one and two dimensional TLC in a range of solvent systems. A glycosylated lipid from WAg200, with separation properties similar to glycosylphenolphthiocerol dimycocerosate was absent or just detectable in WAg533. This observation was supported by the independent isolation of a second colony morphology mutant, WAg537, derived from WAg201, another virulent M. bovis strain. WAg537, like WAg533, also carried an insertional disruption of Rv0097 and showed dramatically reduced production of the same glycosylated lipid. Thus, disruption of Rv0097 causes altered synthesis of a glycosylated cell wall lipid and results in loss of virulence.

L5 ANSWER 22 OF 62 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
AN 2003:574216 BIOSIS
DN PREV200300577041
TI Molecular characterization of the eis promoter of Mycobacterium tuberculosis.
AU Roberts, E. A. [Reprint Author]; Friedman, R. L. [Reprint Author]
CS University of Arizona, Tucson, AZ, USA
SO Abstracts of the General Meeting of the American Society for Microbiology, (2003) Vol. 103, pp. U-070. http://www.asmusa.org/mtgsrc/generalmeeting.htm. cd-rom.
Meeting Info.: 103rd American Society for Microbiology General Meeting. Washington, DC, USA. May 18-22, 2003. American Society for Microbiology. ISSN: 1060-2011 (ISSN print).

DT Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LA English
ED Entered STN: 10 Dec 2003
Last Updated on STN: 10 Dec 2003
AB Our current understanding of Mycobacterium tuberculosis pathogenesis is limited and necessitates further research. This is especially true of our understanding of the expression and regulation of potential virulence genes. In previous studies, the eis gene from M. tuberculosis was shown to enhance the intracellular survival of the avirulent species Mycobacterium smegmatis in the human macrophage-like cell line U-937. In subsequent work, we were able to show that a 412 base pair region of the eis promoter was necessary for maximal expression in M. smegmatis and have now confirmed the same to be true for M. tuberculosis H37Ra (unpublished data). In this study, we attempt to examine and characterize the eis promoter at the molecular level. The transcriptional start point (TSP) of eis was identified using primer extension analysis and found to map to a "G" nucleotide thirty-one nucleotides upstream from the initiation codon. This nucleotide is ten base pairs downstream of the putative -10 region, which matches 4 of 6 nucleotides with the E. coli sigma 70-10 consensus sequence. A putative -35 region exists thirteen base pairs upstream from the -10 region that matches 5 of 6 nucleotides to the E. coli sigma 70 consensus sequence for this region. Primer-based mutagenesis of the putative -10 region coupled with fluorescence analysis yielded an up-mutation demonstrating its importance for transcriptional activity. These data place the eis promoter among the Group A mycobacterial promoters. Error-prone PCR-based mutagenesis of the 412 base pair eis promoter is being performed to further examine and delineate nucleotides essential for eis transcription in both M. smegmatis and M. tuberculosis H37Ra.

L5 ANSWER 23 OF 62 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
AN 2003:556248 BIOSIS
DN PREV200300556959
TI Role of isocitrate lyases in growth and persistence of Mycobacterium tuberculosis in mice and macrophages.
AU Munoz-Elias, E. J. [Reprint Author]; Chan, W. [Reprint Author]; Rice, R. [Reprint Author]; Timm, J. [Reprint Author]; Mirkovic, N. [Reprint Author]; Sali, A. [Reprint Author]; McKinney, J. D. [Reprint Author]
CS Rockefeller University, New York, NY, USA
SO Abstracts of the General Meeting of the American Society for Microbiology, (2003) Vol. 103, pp. U-016. http://www.asmusa.org/mtgsrc/generalmeeting.htm. cd-rom.
Meeting Info.: 103rd American Society for Microbiology General Meeting. Washington, DC, USA. May 18-22, 2003. American Society for Microbiology. ISSN: 1060-2011 (ISSN print).
DT Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LA English
ED Entered STN: 26 Nov 2003
Last Updated on STN: 26 Nov 2003
AB Mycobacterium tuberculosis (MTB) establishes a chronic infection in the face of acquired immunity. We reported previously that isocitrate lyase 1(ICL1), an enzyme involved in fatty acid catabolism, is required for MTB persistence in C57Bl/6 mice; and showed that IFNgamma drives the dependence on ICL1. Here, we demonstrate the role of acquired immunity in this phenomenon using Rag1-/- mice. Rag1-/- mice were highly susceptible to MTB and died within 3 wks after i.v. infection with 106 CFU. The DELTAicl1bacteria replicated efficiently in the RAG1-/- mice and killed them with only slightly delayed kinetics as compared to wild-type bacteria. To investigate the involvement of other immune components, we infected TNFRI-/-, NOS2-/- and PHOX-/- mice with the DELTAicl1

mutant. TNFRI was found to be important for MTB's dependence on ICL1, whereas NOS2 and PHOX appeared not to play a significant role. We also found that the DELTAicl1 mutant is rendered avirulent by deletion of icl2 encoding a putative second ICL. Although MTB mutants lacking either ICL1 or ICL2 replicated exponentially in the lungs of C57Bl/6 mice during the first 2 wks of infection, bacteria deficient in both ICL1 and ICL2 failed to grow and were eradicated from the lungs by 2 wks. DELTAicl1/DELTAicl2 bacteria were also incapable of replication within non-activated mouse or human primary macrophages and were killed by IFNgamma-activated mouse macrophages. In contrast to DELTAicl1 bacteria, the DELTAicl1/DELTAicl2 mutant bacteria were avirulent even in mice lacking IFNgamma or TNFRI. These findings suggest that MTB requires ICL activity for intracellular replication immediately upon entering the macrophage regardless of its activation status and in vivo solely within the context of innate immunity. The partial functional redundancy between the two ICL enzymes agrees with our computer-generated model showing that the structure of the active site is similar in ICL1 and ICL2. Our studies identify an essential metabolic adaptation allowing MTB to infect, replicate, and persist in vivo. We hypothesize that a drug targeting ICL1 and ICL2 would efficiently kill MTB during early and late stages of infection and could shorten TB treatment.

L5 ANSWER 24 OF 62 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN DUPLICATE 11

AN 2002:559623 BIOSIS

DN PREV200200559623

TI Bacterial artificial chromosome-based comparative genomic analysis identifies Mycobacterium microti as a natural ESAT-6 deletion mutant.

AU Brodin, Priscille; Eiglmeier, Karin; Marmiesse, Magali; Billault, Alain; Garnier, Thierry; Niemann, Stefan; Cole, Stewart T.; Brosch, Roland [Reprint author]

CS Unite de Genetique Moleculaire Bacterienne, Institut Pasteur, 28 Rue du Docteur Roux, 75724, Paris Cedex 15, France
rbrosch@pasteur.fr

SO Infection and Immunity, (October, 2002) Vol. 70, No. 10, pp. 5568-5578. print.
CODEN: INFIBR. ISSN: 0019-9567.

DT Article

LA English

ED Entered STN: 30 Oct 2002
Last Updated on STN: 30 Oct 2002

AB Mycobacterium microti is a member of the Mycobacterium tuberculosis complex that causes tuberculosis in voles. Most strains of M. microti are harmless for humans, and some have been successfully used as live tuberculosis vaccines. In an attempt to identify putative virulence factors of the tubercle bacilli, genes that are absent from the avirulent M. microti but present in human pathogen M. tuberculosis or Mycobacterium bovis were searched for. A minimal set of 50 bacterial artificial chromosome (BAC) clones that covers almost all of the genome of M. microti OV254 was constructed, and individual BACs were compared to the corresponding BACs from M. bovis AF2122/97 and M. tuberculosis H37Rv. Comparison of pulsed-field gel-separated DNA digests of BAC clones led to the identification of 10 regions of difference (RD) between M. microti OV254 and M. tuberculosis. A 14-kb chromosomal region (RD1mic) that partly overlaps the RD1 deletion in the BCG vaccine strain was missing from the genomes of all nine tested M. microti strains. This region covers 13 genes, Rv3864 to Rv3876, in M. tuberculosis, including those encoding the potent ESAT-6 and CFP-10 antigens. In contrast, RD5mic, a region that contains three phospholipase C genes (plcA to -C), was missing from only the vole isolates and was present in M. microti strains isolated from humans . Apart from RD1mic and RD5mic other M. microti-specific deleted regions have been identified (MiD1 to MiD3).

Deletion of MiD1 has removed parts of the direct repeat region in M. microti and thus contributes to the characteristic spoligotype of M. microti strains.

L5 ANSWER 25 OF 62 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN DUPLICATE 12
AN 2002:600488 BIOSIS
DN PREV200200600488
TI Production of avirulent mutants of Mycobacterium bovis with vaccine properties by the use of illegitimate recombination and screening of stationary-phase cultures.
AU Collins, D. M. [Reprint author]; Wilson, T.; Campbell, S.; Buddle, B. M.; Wards, B. J.; Hotter, G.; De Lisle, G. W.
CS Wallaceville Animal Research Centre, AgResearch, PO Box 40063, Upper Hutt, New Zealand
desmond.collins@agresearch.co.nz
SO Microbiology (Reading), (October, 2002) Vol. 148, No. 10, pp. 3019-3027. print.
ISSN: 1350-0872.
DT Article
LA English
ED Entered STN: 20 Nov 2002
Last Updated on STN: 20 Nov 2002
AB A better tuberculosis vaccine is urgently required to control the continuing epidemic. Molecular techniques are now available to produce a better live vaccine than BCG by producing avirulent strains of the Mycobacterium tuberculosis complex with known gene deletions. In this study, 1000 illegitimate recombinants of Mycobacterium bovis were produced by illegitimate recombination with fragments of mycobacterial DNA containing a kanamycin resistance gene. Eight recombinant strains were selected on the basis of their inability to grow when stationary-phase cultures were inoculated into minimal medium. Five of these recombinants were found to be avirulent when inoculated into guinea pigs. Two of the avirulent recombinants produced vaccine efficacy comparable to BCG against an aerosol challenge in guinea pigs with M. bovis. One of these recombinants had an inactivated glnA2 gene encoding a putative glutamine synthetase. Transcriptional analysis showed that inactivation of glnA2 did not affect expression of the downstream glnE gene. The other recombinant had a block of 12 genes deleted, including the sigma factor gene sigG. Two avirulent recombinants with an inactivated pckA gene, encoding phosphoenolpyruvate carboxykinase which catalyses the first step of gluconeogenesis, induced poor protection against tuberculosis. It is clear that live avirulent strains of the M. tuberculosis complex vary widely in their ability as vaccines to protect against tuberculosis. Improved models may be required to more clearly determine the difference in protective effect between BCG and potential new tuberculosis vaccines.

L5 ANSWER 26 OF 62 MEDLINE on STN
AN 2002613456 MEDLINE
DN PubMed ID: 12370260
TI Virulent but not avirulent Mycobacterium tuberculosis can evade the growth inhibitory action of a T helper 1-dependent, nitric oxide Synthase 2-independent defense in mice.
AU Jung Yu-Jin; LaCourse Ronald; Ryan Lynn; North Robert J
CS The Trudeau Institute, Saranac Lake, NY 12983, USA.
NC AI-37844 (NIAID)
HL-64565 (NHLBI)
SO The Journal of experimental medicine, (2002 Oct 7) Vol. 196, No. 7, pp. 991-8.
Journal code: 2985109R. ISSN: 0022-1007.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)

(RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LA English
FS Priority Journals
EM 200211
ED Entered STN: 10 Oct 2002
Last Updated on STN: 13 Dec 2002
Entered Medline: 7 Nov 2002
AB Control of infection with virulent Mycobacterium tuberculosis (Mtb) in mice is dependent on the generation of T helper (Th)1-mediated immunity that serves, via secretion of interferon (IFN)-gamma and other cytokines, to upregulate the antimycobacterial function of macrophages of which the synthesis of inducible nitric oxide synthase (NOS)2 is an essential event. As a means to understanding the basis of Mtb virulence, the ability of gene-deleted mice incapable of making NOS2 (NOS2(-/-)), gp91(Phox) subunit of the respiratory burst NADPH-oxidase complex (Phox(-/-)), or either enzyme (NOS2/Phox(-/-)), to control airborne infection with the avirulent R1Rv and H37Ra strains of Mtb was compared with their ability control infection with the virulent H37Rv strain. NOS2(-/-), Phox(-/-), and NOS2/Phox(-/-) mice showed no deficiency in ability to control infection with either strain of avirulent Mtb. By contrast, NOS2(-/-) mice, but not Phox(-/-) mice, were incapable of controlling H37Rv infection and died early from neutrophil-dominated lung pathology. Control of infection with avirulent, as well as virulent Mtb, depended on the synthesis of IFN-gamma, and was associated with a substantial increase in the synthesis in the lungs of mRNA for IFN-gamma and NOS2, and with production of NOS2 by macrophages at sites of infection. The results indicate that virulent, but not avirulent, Mtb can overcome the growth inhibitory action of a Th1-dependent, NOS2-independent mechanism of defense.

L5 ANSWER 27 OF 62 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
AN 2002:609000 BIOSIS
DN PREV200200609000
TI Analysis of the eis promoter of Mycobacterium tuberculosis using transcriptional fusions to gfp and flow cytometry.
AU Roberts, E. A. [Reprint author]; Friedman, R. L. [Reprint author]
CS University of Arizona, Tucson, AZ, USA
SO Abstracts of the General Meeting of the American Society for Microbiology, (2002) Vol. 102, pp. 481. print.
Meeting Info.: 102nd General Meeting of the American Society for Microbiology. Salt Lake City, UT, USA. May 19-23, 2002. American Society for Microbiology.
ISSN: 1060-2011.
DT Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LA English
ED Entered STN: 27 Nov 2002
Last Updated on STN: 27 Nov 2002
AB Background: Our current understanding of Mycobacterium tuberculosis pathogenesis is limited and necessitates further research. This is especially true when pertaining to the expression and regulation of potential virulence genes. Recently, the eis gene from M. tuberculosis was shown to enhance the intracellular survival of the avirulent species Mycobacterium smegmatis in the human macrophage-like cell line U-937. The work presented here examines the in vitro expression of GFP (Green Fluorescent Protein) from variable regions of the eis promoter in M. smegmatis and M. tuberculosis H37Ra. Methods: Variable regions of the eis promoter were PCR amplified and cloned into the promoterless gfp vector pFPV27. The variable promoter clones (pEP922, pEP662, pEP412, and pEP112) were then electroporated into M. smegmatis and H37Ra. Cells were grown to mid-log phase in supplemented 7H9 liquid media, samples were diluted, and then examined by flow cytometry. Cells harboring pFPV27 and pBEN, a vector that expresses gfp from phsp60, were

used as negative and positive controls, respectively. Results: The flow cytometry results show that the eis promoter constructs in M. smegmatis all exhibit approximately 10 to 30-fold higher levels of fluorescence as compared to the negative control. Interestingly, different results were obtained in M. tuberculosis H37Ra. The largest construct, pEP922, produced a 50-fold higher level of fluorescence as compared to pFPV27. In contrast, the fluorescence of pEP662 fell to negative control levels, while pEP412 showed fluorescence levels comparable to pEP922. In cells containing pEP112, fluorescence plummeted to negative control levels. Mutations in the putative -10 region of the eis promoter completely abrogated transcriptional activity, demonstrating this regions essential role. Conclusion: In summary, these results show that the eis promoter is a strong mycobacterial promoter that seems to be constitutively utilized by M. smegmatis. In the native host M. tuberculosis, however, it appears that various regions of the eis promoter may be involved in positive and/or negative transcriptional regulatory functions.

L5 ANSWER 28 OF 62 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2001:208420 CAPLUS
DN 134:247979
TI Virulence genes of Mycobacterium marinum and M. tuberculosis, avirulent mutant mycobacteria and attenuated vaccines
IN Trucksis, Michele
PA University of Maryland, Baltimore, USA; United States Government, as Represented by Department of Veterans Affairs
SO PCT Int. Appl., 99 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001019993	A2	20010322	WO 2000-US25512	20000918
	WO 2001019993	A3	20011122		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	US 2003236393	A1	20031225	US 2003-394575	20030324
	US 2007020287	A1	20070125	US 2005-228203	20050919
PRAI	US 1999-154322P	P	19990917		
	WO 2000-US25512	A	20000918		
	US 2002-366262P	P	20020322		
	US 2002-367206P	P	20020326		
	US 2002-88356	B1	20020722		

AB Methods for identifying, isolating and mutagenizing virulence genes of mycobacteria, e.g., Mycobacterium marinum and M. tuberculosis, are described. The M. marinum signature-tagged mutant library was generated and screened for mutants which exhibit a reduced ability to survive in the goldfish model. Wild type M. marinum virulence genes which correspond to the genes disrupted by transposon in avirulent mutants were isolated. M. tuberculosis genes homologous to M. marinum virulence genes were isolated and characterized. Also described are isolated virulence genes and fragments of them, isolated gene products and fragments of them, avirulent bacteria in which one or more virulence genes are mutagenized, attenuated vaccines containing such mutant

bacteria, and methods to elicit an immune response in a host, using such mutant bacteria.

L5 ANSWER 29 OF 62 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN DUPLICATE 13
AN 2001:504071 BIOSIS
DN PREV200100504071
TI Silencing of oxidative stress response in Mycobacterium tuberculosis: Expression patterns of ahpC in virulent and avirulent strains and effect of ahpC inactivation.
AU Springer, B.; Master, S.; Sander, P.; Zahrt, T.; McFalone, M.; Song, J.; Papavinasasundaram, K. G.; Colston, M. J.; Boettger, E.; Deretic, V. [Reprint author]
CS Department of Microbiology and Immunology, University of Michigan Medical School, 5641 Medical Science Building II, Ann Arbor, MI, 48109-0620, USA Deretic@umich.edu
SO Infection and Immunity, (October, 2001) Vol. 69, No. 10, pp. 5967-5973. print.
CODEN: INFIBR. ISSN: 0019-9567.
DT Article
LA English
ED Entered STN: 31 Oct 2001
Last Updated on STN: 23 Feb 2002
AB Intracellular pathogens such as Mycobacterium tuberculosis are able to survive in the face of antimicrobial products generated by the host cell in response to infection. The product of the alkyl hydroperoxide reductase gene (ahpC) of M. tuberculosis is thought to be involved in protecting the organism against both oxidative and nitrosative stress encountered within the infected macrophage. Here we report that, contrary to expectations, ahpC expression in virulent strains of M. tuberculosis and Mycobacterium bovis grown in vitro is repressed, often below the level of detection, whereas expression in the avirulent vaccine strain M. bovis BCG is constitutively high. The repression of the ahpC gene of the virulent strains is independent of the naturally occurring lesions of central regulator oxyR. Using a green fluorescence protein vector (gfp)-ahpC reporter construct we present data showing that repression of ahpC of virulent M. tuberculosis also occurred during growth inside macrophages, whereas derepression in BCG was again seen under identical conditions. Inactivation of ahpC on the chromosome of M. tuberculosis by homologous recombination had no effect on its growth during acute infection in mice and did not affect in vitro sensitivity to H2O2. However, consistent with AhpC function in detoxifying organic peroxides, sensitivity to cumene hydroperoxide exposure was increased in the ahpC::Kmr mutant strain. The preservation of a functional ahpC gene in M. tuberculosis in spite of its repression under normal growth conditions suggests that, while AhpC does not play a significant role in establishing infection, it is likely to be important under certain, as yet undefined conditions. This is supported by the observation that repression of ahpC expression in vitro was lifted under conditions of static growth.

L5 ANSWER 30 OF 62 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN DUPLICATE 14
AN 2001:141726 BIOSIS
DN PREV200100141726
TI Characterization of auxotrophic mutants of Mycobacterium tuberculosis and their potential as vaccine candidates.
AU Smith, Debbie A. [Reprint author]; Parish, Tanya; Stoker, Neil G.; Bancroft, Gregory J.
CS Department of Infectious and Tropical Diseases, London School of Hygiene and Tropical Medicine, Keppel St., London, WC1E 7HT, UK d.smith@lshtm.ac.uk
SO Infection and Immunity, (February, 2001) Vol. 69, No. 2, pp. 1142-1150. print.

CODEN: INFIBR. ISSN: 0019-9567.
DT Article
LA English
ED Entered STN: 21 Mar 2001
Last Updated on STN: 15 Feb 2002
AB Auxotrophic mutants of Mycobacterium tuberculosis have been proposed as new vaccine candidates. We have analyzed the virulence and vaccine potential of M. tuberculosis strains containing defined mutations in genes involved in methionine (metB), proline (proC), or tryptophan (trpD) amino acid biosynthesis. The metB mutant was a prototrophic strain, whereas the proC and trpD mutants were auxotrophic for proline and tryptophan, respectively. Following infection of murine bone marrow-derived macrophages, H37Rv and the metB mutant strain survived intracellularly for over 10 days, whereas over 90% of proC and trpD mutants were killed during this time. In SCID mice, both H37Rv and the metB mutant were highly virulent, with mouse median survival times (MST) of 28.5 and 42 days, respectively. The proC mutant was significantly attenuated (MST, 130 days), whereas the trpD mutant was essentially avirulent in an immunocompromised host. Following infection of immunocompetent DBA mice with H37Rv, mice survived for a median of 83.5 days and the metB mutant now showed a clear reduction in virulence, with two of five infected mice surviving for 360 days. Both proC and trpD mutants were avirulent (MST of >360 days). In vaccination studies, prior infection with either the proC or trpD mutant gave protection equivalent (proC mutant) to or better (trpD mutant) than BCG against challenge with M. tuberculosis H37Rv. In summary, proC and trpD genes are essential for the virulence of M. tuberculosis, and mutants with disruptions in either of these genes show strong potential as vaccine candidates.

L5 ANSWER 31 OF 62 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN DUPLICATE 15
AN 2001:359894 BIOSIS
DN PREV200100359894
TI Intracellular trafficking of Mycobacterium avium ss. paratuberculosis in macrophages.
AU Cheville, N. F. [Reprint author]; Hostetter, J.; Thomsen, B. V.; Simutis, F.; Vanloubbeeck, Y.; Steadham, E.
CS Department of Veterinary Pathology, Iowa State University, Ames, IA, 50010, USA
nchevill@iastate.edu
SO DTW (Deutsche Tieraerztliche Wochenschrift), (Juni, 2001) Vol. 108, No. 6, pp. 236-243. print.
CODEN: DDTWDG. ISSN: 0341-6593.
DT Article
LA English
ED Entered STN: 2 Aug 2001
Last Updated on STN: 19 Feb 2002
AB The granulomatous enteric lesions of cattle with Johne's disease are composed of infected macrophages, and grow by accumulation, re-infection, and expansion of macrophage populations in the intestinal wall. We have examined the growth of bacteria in macrophages to define characteristics of intracellular trafficking for exocytosis, replication, and antigen presentation. Using immunocytochemical markers for light, confocal and electron microscopy, we have examined potential pathway tropisms using data for bacterial attachment, phagosomal acidification, phagolysosomal degradation and apoptosis. Our hypotheses are that pathogenic/wild-type strains block phagosomal acidification so that the phagosome fails to obtain markers of the late phagosome and phagolysosome, and this leads to the replication pathway within bacteriophorous vacuoles. Non-pathogenic strains appear to be processed to exocytosis, and avirulent mutant strains may be degraded and have preference of antigen processing pathways that involve transport vesicles bearing MHC II

antigens. Pathogenicity in a nude mouse model of intestinal infection reveals lesion development and confirms pathway preferences of virulent strains for bacteriophorous vacuole formation.

L5 ANSWER 32 OF 62 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2002:211028 CAPLUS
DN 137:211652
TI The ESAT-6 gene cluster of Mycobacterium tuberculosis and other high G + C Gram-positive bacteria
AU Van Pittius, Nico C. Gey; Gamieldien, Junaid; Hide, Winston; Brown, Gordon D.; Siezen, Roland; Beyers, Albert D.
CS Dep. Medical Biochemistry, Univ. Stellenbosch, Tygerberg, 7505, S. Afr.
SO GenomeBiology [online computer file] (2001), 2(10), No pp. given
CODEN: GNBLFW; ISSN: 1465-6914
URL: http://genomebiology.com/2001/2/10/research/0044
PB BioMed Central Ltd.
DT Journal; (online computer file)
LA English
AB Background: The genome of Mycobacterium tuberculosis H37Rv has five copies of a cluster of genes known as the ESAT-6 loci. These clusters contain members of the CFP-10 (lhp) and ESAT-6 (esat-6) gene families (encoding secreted T-cell antigens that lack detectable secretion signals) as well as genes encoding secreted, cell-wall-associated subtilisin-like serine proteases, putative ABC transporters, ATP-binding proteins and other membrane-associated proteins. These membrane-associated and energy-providing proteins may function to secrete members of the ESAT-6 and CFP-10 protein families, and the proteases may be involved in processing the secreted peptide. Results: Finished and unfinished genome sequencing data of 98 publicly available microbial genomes has been analyzed for the presence of orthologs of the ESAT-6 loci. The multiple duplicates of the ESAT-6 gene cluster found in the genome of M. tuberculosis H37Rv are also conserved in the genomes of other mycobacteria, for example M. tuberculosis CDC1551, M. tuberculosis 210, M. bovis, M. leprae, M. avium, and the avirulent strain M. smegmatis. Phylogenetic analyses of the resulting sequences have established the duplication order of the gene clusters and demonstrated that the gene cluster known as region 4 (Rv3444c-3450c) is ancestral. Region 4 is also the only region for which an ortholog could be found in the genomes of Corynebacterium diphtheriae and Streptomyces coelicolor. Conclusions: Comparative genomic anal. revealed that the presence of the ESAT-6 gene cluster is a feature of some high-G+C Gram-pos. bacteria. Multiple duplications of this cluster have occurred ad are maintained only within the genomes of members of the genus Mycobacterium.
RE.CNT 56 THERE ARE 56 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 33 OF 62 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2000:900812 CAPLUS
DN 134:70356
TI Avirulent brucella with mutated BacA gene and its uses as vaccines
IN Levier, Kristin; Walker, Graham C.; Roop, Roy M., II; Phillips, Robert W.; Robertson, Gregory T.
PA Massachusetts Institute of Technology, USA
SO PCT Int. Appl., 37 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000077213	A2	20001221	WO 2000-US15949	20000609
	WO 2000077213	A3	20010705		

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU,

CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRAI US 1999-138751P P 19990611

AB The present invention discloses a novel approach to attenuating bacteria and their us as live vaccines. In particular, there is disclosed a method of attenuating bacteria Brucella (B.) abortus by mutating bacA gene, which encodes a membrane protein. The amino acid alignment of BacA from B. abortus, the BacA homolog of R. meliloti, and SbmA from E. coli are provided. The invention also relates to constructing BacA gene expression vector and mutagenesis of BacA gene for preparation avirulent Brucella strain used as vaccines. The invention also discloses methods of deliver compds. into cells by BacA mediated transport and drug screening methods by identifying BacA ligands.

L5 ANSWER 34 OF 62 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2000:145063 CAPLUS
DN 132:204002
TI Molecular differences between species of the M. tuberculosis complex
IN Behr, Marcel; Small, Peter; Schoolnik, Gary; Wilson, Michael A.
PA The Board of Trustees of the Leland Stanford Junior University, USA
SO PCT Int. Appl., 38 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000011214	A1	20000302	WO 1999-US17939	19990810
	W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW				
	RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	US 6291190	B1	20010918	US 1999-318191	19990525
	AU 9953946	A	20000314	AU 1999-53946	19990810
	EP 1108060	A1	20010620	EP 1999-939702	19990810
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	US 2006002953	A1	20060105	US 2005-143401	20050601
PRAI	US 1998-97936P	P	19980825		
	US 1999-318191	A	19990525		
	WO 1999-US17939	W	19990810		
	US 2001-894844	A1	20010627		
	US 2003-647089	B1	20030821		

AB Specific genetic deletions are identified in mycobacteria isolates, including variations in the M. tuberculosis genome sequence between isolates, and numerous deletion present in BCG as compared to M. tb. These deletions are used as markers to distinguish between pathogenic and avirulent strains, and as a marker for particular M. tb isolates. Deletions specific to vaccine strains of BCG are useful in determining whether a pos. tuberculin skin test is indicative of actual tuberculosis infection. The deleted sequences may be re-introduced into BCG to improve the efficacy of vaccination. Alternatively, the genetic sequence that corresponds to the deletion(s) is deleted from M. bovis or M. tuberculosis to attenuate the pathogenic bacteria. A convenient

listing of deletion markers is condensed in table I. A genetically altered mycobacterium is prepared with a physiol. acceptable carrier for injection for vaccination. Homologous recombination is used to generate a deletion in deletion marker. These genetic markers are used for assays such as immunoassays, that distinguish between strains, such as to differentiate between BCG immunization and M. tb. infection. The protein products may be produced and used as immunogen, in drug screening, etc.

RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 35 OF 62 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN DUPLICATE 16

AN 2000:218451 BIOSIS

DN PREV200000218451

TI Deviant expression of Rab5 on phagosomes containing the intracellular pathogens Mycobacterium tuberculosis and Legionella pneumophila is associated with altered phagosomal fate.

AU Clemens, Daniel L. [Reprint author]; Lee, Bai-Yu; Horwitz, Marcus A.

CS Division of Infectious Diseases, Department of Medicine, Center for Health Sciences, UCLA School of Medicine, Los Angeles, CA, 90095, USA

SO Infection and Immunity, (May, 2000) Vol. 68, No. 5, pp. 2671-2684. print. CODEN: INFIBR. ISSN: 0019-9567.

DT Article

LA English

ED Entered STN: 31 May 2000
Last Updated on STN: 5 Jan 2002

AB The intracellular human pathogens Legionella pneumophila and Mycobacterium tuberculosis reside in altered phagosomes that do not fuse with lysosomes and are only mildly acidified. The L. pneumophila phagosome exists completely outside the endolysosomal pathway, and the M. tuberculosis phagosome displays a maturational arrest at an early endosomal stage along this pathway. Rab5 plays a critical role in regulating membrane trafficking involving endosomes and phagosomes. To determine whether an alteration in the function or delivery of Rab5 could play a role in the aberrant development of L. pneumophila and M. tuberculosis phagosomes, we have examined the distribution of the small GTPase, Rab5c, in infected HeLa cells overexpressing Rab5c. Both pathogens formed phagosomes in HeLa cells with molecular characteristics similar to their phagosomes in human macrophages and multiplied in these host cells. Phagosomes containing virulent wild-type L. pneumophila never acquired immunogold staining for Rab5c, whereas phagosomes containing an avirulent mutant L. pneumophila (which ultimately fused with lysosomes) transiently acquired staining for Rab5c after phagocytosis. In contrast, M. tuberculosis phagosomes exhibited abundant staining for Rab5c throughout its life cycle. To verify that the overexpressed, recombinant Rab5c observed on the bacterial phagosomes was biologically active, we examined the phagosomes in HeLa cells expressing Rab5c Q79L, a fusion-promoting mutant. Such HeLa cells formed giant vacuoles, and after incubation with various particles, the giant vacuoles acquired large numbers of latex beads, M. tuberculosis, and avirulent L. pneumophila but not wild-type L. pneumophila, which consistently remained in tight phagosomes that did not fuse with the giant vacuoles. These results indicate that whereas Rab5 is absent from wild-type L. pneumophila phagosomes, functional Rab5 persists on M. tuberculosis phagosomes. The absence of Rab5 on the L. pneumophila phagosome may underlie its lack of interaction with endocytic compartments. The persistence of functional Rab5 on the M. tuberculosis phagosomes may enable the phagosome to retard its own maturation at an early endosomal stage.

L5 ANSWER 36 OF 62 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN DUPLICATE 17

AN 2001:241233 BIOSIS

DN PREV200100241233
TI Population genetics of nodule bacteria.
AU Provorov, N. A. [Reprint author]
CS All-Russia Research Institute for Agricultural Microbiology, Russian Academy of Agricultural Sciences, Podbelsky Sh. 3, Saint Petersburg, 189620, Russia
SO Zhurnal Obshchei Biologii, (May-June, 2000) Vol. 61, No. 3, pp. 229-257. print.
CODEN: ZOBIAU. ISSN: 0044-4596.
DT Article
General Review; (Literature Review)
LA Russian
ED Entered STN: 16 May 2001
Last Updated on STN: 19 Feb 2002
AB The data are reviewed on the population structure and evolutionary dynamics of the nodule bacteria (rhizobia) which are among the most intensively studied microorganisms. High level of the population polymorphism was demonstrated for the rhizobia populations using the enzyme electrophoresis (MLEE profiles). The average value of Nei's coefficient of heterogeneity (H = 1 - sumpi2 (n / (n - 1))) were: 0,590 for rhizobia (Rhizobium, Bradyrhizobium), 0,368 for enterobacteria (Escherichia, Salmonella, Shigella) and 0,452 for pathogenic bacteria (Bordetella, Borrelia, Eryispelotrix, Haemophilus, Heliobacter, Listeria, Mycobacterium, Neisseria, Staphylococcus) populations. In spite of being devoid of the effective systems for the gene conjugative transfer, many rhizobia populations possess an essentially panmictic structure. However, the enterobacteria populations in which the gene transfer may be facilitated due to the conjugative F- and R-factors, usually display the clonal population structure. The legume host plant is proved to be a key factor that determines the high levels of polymorphism and of panmixia as well as high evolutionary rates of the symbiotic bacteria populations. The host may ensure: a) an increase in mutation and gene transfer frequencies; b) stimulation of the competitive (selective) processes in both symbiotic and free-living rhizobia populations. A "cyclic" model of the rhyzobia microevolution is presented which allows to assess the inputs the interstrain competition for the saprophytic growth and for the host nodulation into evolution of a plant-associated rhizobia population. The nodulation competitiveness in the rhizobia populations is responsible for the frequency-dependent selection of the rare genotypes which may arise in the soil bacterial communities as a result of the transfer of symbiotic (sym) genes from virulent rhizobia strains to either avirulent rhizobia or to the other (saprophytic, phytopathogenic) bacteria. Therefore, the nodulation competitiveness may ensure: a) panmictic structure of the natural rhizobia populations; b) high taxonomic diversity of rhizobia which was apparently caused by a broad sym gene expansion in the soil bacterial communities. The kin selection models are presented which explain evolution of the "altruistic" (essential for the host plant, but not for the bacteria themselves) symbiotic traits (e.g., the ability for symbiotic nitrogen fixation and for differentiation into non-viable bacteroids) in the rhizobia populations. These models are based on preferential multiplication of the nitrogen-fixing clones either in planta (due to an elevated supply of the nitrogen-fixing nodules with photosynthates) or ex planta (due to a release of the rhizopines from the nitrogen-fixing nodules). Speaking generally, interactions with the host plants provide a range of mechanisms increasing a genetic heterogeneity and an evolutionary potential in the associated rhizobia populations.

L5 ANSWER 37 OF 62 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2000:843515 CAPLUS
DN 134:46685
TI Attenuated strains of Mycobacterium, Vibrio, Shigella and Listeria as a polyvalent vaccines
AU Pawelec, Dariusz Piotr; Jagusztyn-Krynicka, Elzbieta Katarzyna

CS Inst. Mikrobiol. Zaklad Genet. Bakterii, UW, Warsaw, 00-046, Pol.
SO Postepy Mikrobiologii (2000), 39(2), 155-175
CODEN: PMKMAV; ISSN: 0079-4252
PB Polskie Towarzystwo Mikrobiologow
DT Journal
LA Polish
AB Pathogenic bacteria can be attenuated and engineered into live recombinant vectors for expressing the polypeptides encoded by other microorganisms. The use of recombinant avirulent BCG, Vibrio cholerae and Shigella flexneri as a live vehicles appears to offer a safe and efficacious means of immunizing individuals against a diversity of infectious disease agents. Listeria monocytogenes, an opportunistic pathogen, is also taken into account as a delivery vector. This review presents the features of the currently constructed avirulent mutants of the particular microorganisms. It also concs. on various methods employed for foreign gene cloning and expression, as well as on different aspects of the gene products immunogenicity evaluated on animal models. In addition, several limitations concerning the use of the constructed strains as human vaccine are summarized below.

L5 ANSWER 38 OF 62 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN DUPLICATE 18
AN 1999:446727 BIOSIS
DN PREV199900446727
TI Preliminary characterization of a Mycobacterium abscessus mutant in human and murine models of infection.
AU Byrd, Thomas F. [Reprint author]; Lyons, C. Rick
CS Department of Medicine (111J), Albuquerque Veterans Affairs Medical Center, 1501 San Pedro, SE, Albuquerque, NM, 87108, USA
SO Infection and Immunity, (Sept., 1999) Vol. 67, No. 9, pp. 4700-4707. print.
CODEN: INFIBR. ISSN: 0019-9567.
DT Article
LA English
ED Entered STN: 26 Oct 1999
Last Updated on STN: 26 Oct 1999
AB The ability to persist in the host after the establishment of infection is an important virulence determinant for mycobacteria. Mycobacterium abscessus is a rapidly growing mycobacterial species which causes a variety of clinical syndromes in humans. We have obtained a rough, wild-type human clinical isolate of M. abscessus (M. abscessus-R) and a smooth, attenuated mutant (M. abscessus-S) which spontaneously dissociated from the clinical isolate. We have found that M. abscessus-R is able to persist and multiply in a murine pulmonary infection model in contrast to M. abscessus-S, which is rapidly cleared. To understand the basis for this difference, we characterized the behavior of these variants in human tissue culture models of infection. M. abscessus-R is able to persist and multiply in human monocytes, while M. abscessus-S is deficient in this ability. Both of these variants are phagocytized by human monocytes. M. abscessus-R resides in a phagosome typical for pathogenic mycobacteria with a tightly adherent phagosomal membrane. In contrast, M. abscessus-S resides in a "loose" phagosome with the phagosomal membrane separated from the bacterial cell wall. Both M. abscessus variants also have distinctive growth patterns in a recently described fibroblast-mycobacterium microcolony assay, with M. abscessus-R exhibiting growth characteristics similar to those previously reported for virulent M. tuberculosis and M. abscessus-S exhibiting growth characteristics similar to those previously reported for avirulent M. tuberculosis. In both the monocyte infection assay and the murine pulmonary infection model, numerous infected mononuclear phagocyte aggregates develop at sites of M. abscessus-R infection, but are absent with M. abscessus-S infection. We conclude that a mutation has occurred in the M. abscessus-S variant which has altered the ability of this organism to persist and multiply in host cells and that this may

be related to the phenotypic changes we have observed in our tissue culture models of infection.

L5 ANSWER 39 OF 62 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN DUPLICATE 19
AN 1999:264242 BIOSIS
DN PREV199900264242
TI Vaccination of guinea pigs with nutritionally impaired avirulent mutants of Mycobacterium bovis protects against tuberculosis.
AU de Lisle, Geoffrey W. [Reprint author]; Wilson, Theresa; Collins, Desmond M.; Buddle, Bryce M.
CS Wallaceville Animal Research Centre, AgResearch, Upper Hutt, New Zealand
SO Infection and Immunity, (May, 1999) Vol. 67, No. 5, pp. 2624-2626. print. CODEN: INFIBR. ISSN: 0019-9567.
DT Article
LA English
ED Entered STN: 15 Jul 1999
Last Updated on STN: 15 Jul 1999
AB Four nutritionally impaired strains or Mycobacterium bovis produced by illegitimate recombination were tested for their ability to protect guinea pigs against intratracheal challenge with virulent M. bovis. All four strains and M. bovis BCG induced significant levels of protection as measured by the reduced spread of infection to the spleen and liver. In animals vaccinated with BCG or two of the other strains, the bacterial counts from the lungs were significantly lower than those of the nonvaccinated animals.

L5 ANSWER 40 OF 62 LIFESCI COPYRIGHT 2007 CSA on STN
AN 1999:73261 LIFESCI
TI Vaccination of guinea pigs with nutritionally impaired avirulent mutants of Mycobacterium bovis protects against tuberculosis
AU De Liste, G.W.; Wilson, Th.; Collins, D.M.; Buddle, B.M.
CS AgResearch, Wallaceville Animal Research Centre, P.O. Box 40-063, Upper Hutt, New Zealand; E-mail: delisleg@agresearch.cri.nz
SO Infection and Immunity [Infect. Immun.], (19990500) vol. 65, no. 5, pp. 2624-2626.
ISSN: 0019-9567.
DT Journal
FS J; F
LA English
SL English
AB Four nutritionally impaired strains of Mycobacterium bovis produced by illegitimate recombination were tested for their ability to protect guinea pigs against intratracheal challenge with virulent M. bovis. All four strains and M. bovis BCG induced significant levels of protection as measured by the reduced spread of infection to the spleen and liver. In animals vaccinated with BCG or two of the other strains, the bacterial counts from the lungs were significantly lower than those of the nonvaccinated animals.

L5 ANSWER 41 OF 62 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN DUPLICATE 20
AN 1999:281279 BIOSIS
DN PREV199900281279
TI IS6110-based restriction fragment length polymorphism (RFLP) analysis of Mycobacterium tuberculosis H37Rv and H37Ra.
AU Lari, Nicoletta; Rindi, Laura; Lami, Cristiana; Garzelli, Carlo [Reprint author]
CS Dipartimento di Patologia Sperimentale, Biotecnologie, Mediche, Infettivologia ed Epidemiologia, Via San Zeno, 35/39, I-56127, Pisa, Italy
SO Microbial Pathogenesis, (May, 1999) Vol. 26, No. 5, pp. 281-286. print. CODEN: MIPAEV. ISSN: 0882-4010.

DT Article
LA English
ED Entered STN: 28 Jul 1999
Last Updated on STN: 28 Jul 1999
AB IS6110-based restriction fragment length polymorphism (RFLP) analysis of Mycobacterium tuberculosis H37Rv and its avirulent mutant H37Ra was performed by a number of restriction enzymes, including Nru I, EcoN I, Pst I, and Pvu II. No differences were found in the IS6110-fingerprints of the study strains by Nru I. One differential IS6110-positive restriction fragment was detected by EcoN I in strain H37Ra, while analysis by Pst I revealed that two fragments of the strain H37Rv were replaced by four novel IS6110-positive fragments in the strain H37Ra. By using Pvu II, a restriction enzyme that cleaves IS6110 once, and by probing for an IS6110-specific target sequence located to the right of the Pvu II site, we found that the strains H37Rv and H37Ra share 13 IS6110-positive restriction fragments and that one IS6110-positive restriction fragment of H37Rv is replaced by four novel fragments in H37Ra; by probing for an IS6110-specific target sequence to the left of the Pvu II site, 13 shared restriction fragments and 2 differential bands in strain H37Ra were detected. These findings demonstrate that novel insertions of the IS6110 element exist in the avirulent strain H37Ra and raise the question of the role, if any, of IS6110-insertional mutagenesis in the establishment of the avirulent M. tuberculosis H37Ra phenotype.

L5 ANSWER 42 OF 62 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN. DUPLICATE 21
AN 1999:263560 BIOSIS
DN PREV199900263560
TI Search for genes potentially involved in Mycobacterium tuberculosis virulence by mRNA differential display.
AU Rindi, Laura [Reprint author]; Lari, Nicoletta [Reprint author]; Garzelli, Carlo [Reprint author]
CS Dipartimento di Patologia Sperimentale, Biotecnologie Mediche, Infettivologia ed Epidemiologia, Universita di Pisa, I-56127, Pisa, Italy
SO Biochemical and Biophysical Research Communications, (April 29, 1999) Vol. 258, No. 1, pp. 94-101. print.
CODEN: BBRCA9. ISSN: 0006-291X.
DT Article
LA English
ED Entered STN: 15 Jul 1999
Last Updated on STN: 15 Jul 1999
AB An mRNA differential display (DD) assay was developed to compare gene expression between Mycobacterium tuberculosis H37Rv and its avirulent mutant H37Ra. The DD protocol made use of an oligo(dT) to prime reverse-transcriptase (RT)-dependent transcription of poly-A tailed mRNAs and a PCR amplification of the RT products by using ten 12-base arbitrary primers in all their pair combinations. This analysis yielded 745 and 708 bands, including 52 and 15 differentially generated bands, in the strains H37Rv and H37Ra, respectively. Six cDNAs that appeared to be expressed in H37Rv, but not in H37Ra, were reamplified and cloned and at least 10 inserts were sequenced for each cloned cDNA. After resolving discrepant results, 6 inserts were found highly homologous to M. tuberculosis H37Rv genes. Three of these, i.e., genes Rv2770c, Rv1345, and Rv0288, coding respectively for a member of the PPE protein family, a probable polyketide synthase, and a member of the protein family containing ESAT-6, have been predictively associated to immunological or pathogenetic aspects of M. tuberculosis infection; the other genes, i.e., Rv2336, Rv1320c, and Rv2819c, code for proteins with unknown functions. These results show that mRNA DD methodology can represent a potential tool for investigation of M. tuberculosis gene expression.

L5 ANSWER 43 OF 62 CAPLUS COPYRIGHT 2007 ACS on STN
AN 1998:493192 CAPLUS

DN 129:120090
TI Virulence factors of Mycobacteria and the genes encoding them and their detection and use
IN Jacobs, William R., Jr.; Bloom, Barry R.; Collins, Desmond Michael; De Lisle, Geoffrey W.; Pascopella, Lisa; Kawakami, Riku Pamela
PA Agresearch, New Zealand Pastoral Agriculture Research Institute Ltd., N. Z.; Albert Einstein College of Medicine of Yeshiva University
SO U.S., 74 pp., Cont.-in-part of U.S. Ser. No. 292,695, abandoned.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 5783386	A	19980721	US 1994-363255	19941223
PRAI	US 1994-201880	B2	19940224		
	US 1994-265579	B2	19940624		
	US 1994-292695	B2	19940818		

AB DNA sequences associated with virulence in Mycobacteria, and particularly a fragment of DNA isolated from M. bovis that contains a region encoding a putative sigma factor are described. These sequences can be used to detect the corresponding DNA sequence or sequences associated with virulence determinants in mycobacteria, and particularly in M. tuberculosis and M. bovis. The invention also provides corresponding polynucleotides associated with avirulence in mycobacteria. Vaccine strains may be generated by directed mutagenesis of the virulence gene. In addition, a method for producing strains with altered virulence or other properties which can themselves be used to identify and manipulate individual genes is described. The method involves converting an avirulent host strain to virulence and measuring the effects in vivo.
RE.CNT 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 44 OF 62 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN DUPLICATE 22
AN 1998:393346 BIOSIS
DN PREV199800393346
TI Site-directed mutagenesis of the 19-kilodalton lipoprotein antigen reveals no essential role for the protein in the growth and virulence of Mycobacterium intracellulare.
AU Mahenthiralingam, Eshwar; Marklund, Britt-Inger; Brooks, Lucy A.; Smith, Debbie A.; Bancroft, Gregory J.; Stokes, Richard W. [Reprint author]
CS Div. Infect. Immunol. Dis., Dep. Pediatrics, Univ. B.C., Room 304, Res. Inst., 950 W. 28th Ave., Vancouver, BC V5Z 4H4, Canada
SO Infection and Immunity, (Aug., 1998) Vol. 66, No. 8, pp. 3626-3634. print.
CODEN: INFIBR. ISSN: 0019-9567.
DT Article
LA English
ED Entered STN: 10 Sep 1998
Last Updated on STN: 10 Sep 1998
AB The mycobacterial 19-kilodalton antigen (19Ag) is a highly expressed, surface-associated glycolipoprotein which is immunodominant in infected patients and has little homology with other known proteins. To investigate the pathogenic significance of the 19Ag, site-directed mutagenesis of the Mycobacterium intracellulare 19Ag gene was carried out by using a suicide vector-based strategy. Allelic replacement of the 19Ag gene of a mouse-avirulent M. intracellulare strain, 1403, was achieved by double-crossover homologous recombination with a gentamicin resistance gene-mutated allele. Unfortunately, an isogenic 19Ag was not achievable in the mouse-virulent strain, D673. However, a 19Ag mutant was successfully constructed in M. intracellulare FM1, a chemically mutagenized derivative of strain D673. FM1 was more amenable to genetic manipulation

and susceptible to site-directed mutagenesis of the 19Ag gene yet retained the virulent phenotype of the parental strain. No deleterious effects of 19Ag gene mutation were observed during in vitro growth of M. intracellulare. Virulence assessment of the isogenic 19Ag mutants in a mouse infection model demonstrated that the antigen plays no essential role in the growth of M. intracellulare in vivo. Site-directed mutagenesis of the 19Ag gene demonstrated that it plays no essential role in growth and pathogenicity of M. intracellulare; however, the exact nature of its biological function remains unknown.

L5 ANSWER 45 OF 62 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN DUPLICATE 23
AN 1996:186861 BIOSIS
DN PREV199698742990
TI Molecular analysis of genetic differences between Mycobacterium bovis BCG and virulent M. bovis.
AU Mahairas, Gregory G.; Sabo, Peter J.; Hickey, Mark J.; Singh, Devinder C.; Stover, C. Kendall [Reprint author]
CS Lab. Molecular Microbiol., PathoGenesis Corp., 101 Elliott Ave. West, Seattle, WA 98119, USA
SO Journal of Bacteriology, (1996) Vol. 178, No. 5, pp. 1274-1282. CODEN: JOBAAY. ISSN: 0021-9193.
DT Article
LA English
ED Entered STN: 29 Apr 1996
Last Updated on STN: 29 Apr 1996
AB The live attenuated bacillus Calmette-Guerin (BCG) vaccine for the prevention of disease associated with Mycobacterium tuberculosis was derived from the closely related virulent tubercle bacillus, Mycobacterium bovis. Although the BCG vaccine has been one of the most widely used vaccines in the world for over 40 years, the genetic basis of BCG's attenuation has never been elucidated. We employed subtractive genomic hybridization to identify genetic differences between virulent M. bovis and M. tuberculosis and avirulent BCG. Three distinct genomic regions of difference (designated RD1 to RD3) were found to be deleted from BCG, and the precise junctions and DNA sequence of each deletion were determined. RD3, a 9.3-kb genomic segment present in virulent laboratory strains of M. bovis and M. tuberculosis, was absent from BCG and 84% of virulent clinical isolates. RD2, a 10.7-kb DNA segment containing a novel repetitive element and the previously identified mpt-64 gene, was conserved in all virulent laboratory and clinical tubercle bacilli tested and was deleted only from substrains derived from the original BCG Pasteur strain after 1925. Thus, the RD2 deletion occurred after the original derivation of BCG. RD1, a 9.5-kb DNA segment found to be deleted from all BCG substrains, was conserved in all virulent laboratory and clinical isolates of M. bovis and M. tuberculosis tested. The reintroduction of RD1 into BCG repressed the expression of at least 10 proteins and resulted in a protein expression profile almost identical to that of virulent M. bovis and M. tuberculosis, as determined by two-dimensional gel electrophoresis. These data indicate a role for RD1 in the regulation of multiple genetic loci, suggesting that the loss of virulence by BCG is due to a regulatory mutation. These findings may be applicable to the rational design of a new attenuated tuberculosis vaccine and the development of new diagnostic tests to distinguish BCG vaccination from tuberculosis infection.

L5 ANSWER 46 OF 62 CAPLUS COPYRIGHT 2007 ACS on STN
AN 1995:820783 CAPLUS
DN 123:222685
TI Virulence factors of Mycobacteria and the genes encoding them and their detection and use
IN Jacobs, William R., Jr.; Bloom, Barry R.; Collins, Desmond Michael; De, Lisle Geoffrey W.; Pascopella, Lisa; Kawakami, Riku Pamela

PA Agresearch New Zealand Pastoral Agriculture Research, N. Z.; Albert Einstein College of Medicine of Yeshiva University
SO PCT Int. Appl., 115 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9517511	A2	19950629	WO 1994-US14912	19941223
	WO 9517511	A3	19950727		
	W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, TJ, TT, UA, US, UZ				
	RW: KE, MW, SD, SZ, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	CA 2179772	A1	19950629	CA 1994-2179772	19941223
	AU 9514458	A	19950710	AU 1995-14458	19941223
	EP 736098	A1	19961009	EP 1995-906122	19941223
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
	JP 09510866	T	19971104	JP 1995-517634	19941223
PRAI	NZ 1993-250584	A	19931223		
	US 1994-201880	A	19940224		
	US 1994-265579	A	19940624		
	US 1994-292695	A	19940818		
	WO 1994-US14912	W	19941223		

AB DNA sequences associated with virulence in Mycobacteria, and particularly a fragment of DNA isolated from M. bovis that contains a region encoding a putative sigma factor are described. These sequences can be used to detect the corresponding DNA sequence or sequences associated with virulence determinants in mycobacteria, and particularly in M. tuberculosis and M. bovis. The invention also provides corresponding polynucleotides associated with avirulence in mycobacteria. Vaccine strains may be generated by directed mutagenesis of the virulence gene. In addition, a method for producing strains with altered virulence or other properties which can themselves be used to identify and manipulate individual genes is described. The method involves converting an avirulent host strain to virulence and measuring the effects in vivo.

L5 ANSWER 47 OF 62 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN DUPLICATE 24
AN 1995:314606 BIOSIS
DN PREV199598328906
TI Increased Gamma-Delta T-Lymphocyte Response to Mycobacterium bovis BCG in Major Histocompatibility Complex Class I-Deficient Mice.
AU Muller, Daniel [Reprint author]; Pakpreo, Ponrat; Filla, Joan; Pederson, Katrina; Cigel, Francine; Malkovska, Vera
CS Div. Rheumatol., Dep. Med., 2605 MSC, 1300 University Ave., University Wisconsin-Madison, Madison, WI 53706, USA
SO Infection and Immunity, (1995) Vol. 63, No. 6, pp. 2361-2366.
CODEN: INFIBR. ISSN: 0019-9567.
DT Article
LA English
ED Entered STN: 30 Jul 1995
Last Updated on STN: 30 Jul 1995
AB Mice with a homologous deletion of the beta-2-microglobulin gene (beta-2m-) are deficient in class I major histocompatibility complex molecules (MHC) and consequently are deficient in CD8+ T cells. These beta-2m- mutant mice control the intraperitoneal growth of an avirulent vaccine strain of mycobacteria, Mycobacterium bovis BCG, after intraperitoneal infection similarly

to normal mice. We show that beta-2m- mice have an increased gamma-delta (gamma-delta) T-cell response after infection with live avirulent mycobacteria. beta-2m- mice have an earlier and more sustained rise in the proportion of intraperitoneal gamma-delta T cells, averaging 17% of T cells, compared with 6% in normal mice, at 28 days after infection. Compared with the population in normal mice, gamma-delta T cells in the spleens of beta-2m- mice averaged a higher proportion of the total T-cell population of the spleen on days 5, 8, and 14 after intraperitoneal infection. These data document the kinetics of gamma-delta T cells reactive to mycobacterial antigens in vivo without class I MHC restriction and support a role for class I MHC and CD8+ T cells in the in vivo regulation of gamma-delta T cells.

L5 ANSWER 48 OF 62 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
AN 1993:501175 BIOSIS
DN PREV199396125182
TI In vitro influence of Listeria on uterine activity.
AU Lechner, W.; Allerberger, F. [Reprint author]; Bergant, A.; Soelder, E.; Dierich, M. P.
CS Dep. Immunol. and Infectious Diseases, Johns Hopkins Univ., 615 North Wolfe St., Baltimore, MD 21205, USA
SO Zeitschrift fuer Geburtshilfe und Perinatologie, (1993) Vol. 197, No. 4, pp. 179-183.
CODEN: ZGPRA3. ISSN: 0300-967X.
DT Article
LA German
ED Entered STN: 5 Nov 1993
Last Updated on STN: 5 Nov 1993
AB In Austria the prevalence of listeriosis is 2.6 cases per million inhabitants yearly, hence rather rarely the cause of spontaneous abortion or premature birth. On the other hand, Listeria monocytogenes is found in 1% of the asymptomatic population as a component of stool flora. Since the cause of premature labor contractions remains unclear in about half of all cases, we examined 29 listeria strains for their ability to cause myometrial contraction by direct contact using an in-vitro uterine strip-model. Seven of nine L. monocytogenes strains were able to cause contractions; contractions were not inducible by an nonhemolytic mutane (SLCC 53, avirulent) nor by a rough strain (SLCC 5779, only slightly virulent). Three of six L. ivanovii isolates also exhibited the ability to induce contractions. None of the pathogenic species (L. innocua, L. seeligeri, L. welshimeri, L. grayi and L. murrayi) was capable of activating contractions in our in-vitro model. Only L. monocytogenes and L. ivanovii cause conjunctivitis after being dropped in rabbit's eyes (positive Anton Test). The influence of listeria on uterine activity as found in our in vitro model thus correlates with the classical pathogenicity test. We consider these in-vitro results as an additional argument to oppose the presence of L. monocytogenes in ready-to-eat foods.

L5 ANSWER 49 OF 62 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN DUPLICATE 25
AN 1993:95240 BIOSIS
DN PREV199395050436
TI Major histocompatibility complex class I-restricted T cells are required for resistance to Mycobacterium tuberculosis infection.
AU Flynn, Joanne L. [Reprint author]; Goldstein, Marsha M.; Triebold, Karla J.; Koller, Beverly; Bloom, Barry R.
CS Howard Hughes Med. Inst., Albert Winstein Coll. Med., Bronx, N.Y. 10461, USA
SO Proceedings of the National Academy of Sciences of the United States of America, (1992) Vol. 89, No. 24, pp. 12013-12017.
CODEN: PNASA6. ISSN: 0027-8424.
DT Article
LA English

ED Entered STN: 9 Feb 1993
Last Updated on STN: 9 Feb 1993

AB Mice with a targeted disruption in the beta-2-microglobulin (beta-2m) gene, which lack major histocompatibility complex class I molecules and consequently fail to develop functional CD8 T cells, provided a useful model for assessing the role of class I-restricted T cells in resistance to infection with virulent Mycobacterium tuberculosis. Of mutant beta-2m-/-mice infected with virulent 10-6 M. tuberculosis, 70% were dead or moribund after 6 weeks, while all control mice expressing the beta-2m gene remained alive for gt 20 weeks. Granuloma formation occurred in mutant and control mice, but far greater numbers of tubercle bacilli were present in the lungs of mutant mice than in controls, and caseating necrosis was seen only in beta-2m-/-lungs. In contrast, no differences were seen in the course of infection of mutant and control mice with an avirulent vaccine strain, bacille Calmette-Guerin (BCG). Immunization with BCG vaccine prolonged survival of beta-2m-/-mice after challenge with M. tuberculosis for 4 weeks but did not protect them from death. These data indicate that functional CD8 T cells, and possibly T cells bearing gamma-delta antigen receptor, are a necessary component of a protective immune response to M. tuberculosis in mice.

L5 ANSWER 50 OF 62 CAPLUS COPYRIGHT 2007 ACS on STN
AN 1989:455685 CAPLUS
DN 111:55685
TI Avirulent microbe vaccines lacking functional adenylate cyclase and cAMP receptor protein, their preparation, and uses therefor
IN Curtiss, Roy, III
PA Molecular Engineering Associates, Inc., USA
SO PCT Int. Appl., 87 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 3

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 8809669	A1	19881215	WO 1988-US1899	19880601
	W: AU, DK, JP, KR				
	RW: AT, BE, CH, DE, FR, GB, IT, LU, NL, SE				
	AU 8819550	A	19890104	AU 1988-19550	19880601
	AU 623599	B2	19920521		
	EP 315682	A1	19890517	EP 1988-905542	19880601
	EP 315682	B1	19931222		
	R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
	JP 01503442	T	19891122	JP 1988-505197	19880601
	JP 2640525	B2	19970813		
	AT 98870	T	19940115	AT 1988-905542	19880601
	CA 1338957	C	19970304	CA 1988-568456	19880602
	ZA 8803954	A	19890222	ZA 1988-3954	19880603
	CN 1030018	A	19890104	CN 1988-104317	19880604
	CN 1034553	B	19970416		
	DK 8900527	A	19890203	DK 1989-527	19890203
	DK 175512	B1	20041115		
	KR 139950	B1	19980601	KR 1989-700206	19890204
	US 5294441	A	19940315	US 1991-785748	19911107
	WO 9208486	A1	19920529	WO 1991-US8376	19911108
	W: AU, CA, JP				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, NL, SE				
	AU 9191204	A	19920611	AU 1991-91204	19911108
	AU 666108	B2	19960201		
	ZA 9108876	A	19920826	ZA 1991-8876	19911108
	EP 556333	A1	19930825	EP 1992-901722	19911108
	EP 556333	B1	20030319		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				

	JP 06501849	T	19940303	JP 1992-502265	19911108
	JP 3601602	B2	20041215		
	IL 100010	A	19980208	IL 1991-100010	19911108
	CA 2095534	C	20020917	CA 1991-2095534	19911108
	AT 234917	T	20030415	AT 1992-901722	19911108
	EP 1323428	A2	20030702	EP 2003-6123	19911108
	EP 1323428	A3	20030917		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
	ES 2194837	T3	20031201	ES 1992-901722	19911108
	CN 1063416	A	19920812	CN 1991-111876	19911109
	US 5389368	A	19950214	US 1992-965607	19921022
	US 5468485	A	19951121	US 1993-20259	19930218
	US 5387744	A	19950207	US 1993-88394	19930707
	US 5855879	A	19990105	US 1994-209542	19940310
	US 5855880	A	19990105	US 1996-596732	19960205
	JP 2004337175	A	20041202	JP 2004-207489	20040714
PRAI	US 1987-58360	A	19870604		
	US 1988-200934		19880601		
	US 1990-612001		19901109		
	US 1987-106072	B2	19871007		
	EP 1988-905542	A	19880601		
	WO 1988-US1899	A	19880601		
	US 1988-251304	B2	19881003		
	US 1989-332285	B1	19890331		
	US 1991-785748	A3	19911107		
	EP 1992-901722	A3	19911108		
	JP 1992-502265	A3	19911108		
	WO 1991-US8376	A	19911108		
	US 1992-975892	B1	19921113		
	US 1994-209542	A3	19940310		

AB A vaccine for immunization of vertebrates or invertebrates comprises an avirulent derivative of a pathogen that is incapable of producing functional adenylate cyclase (AC) and cAMP receptor protein (cRP). The avirulent microbe is produced by recombinant DNA techniques or transposon mutagenesis, forming deletion mutations in each of the genes for AC and cRP. The avirulent microbe is also used as a carrier for synthesis of a vertebrate or invertebrate host protein to produce a product capable of suppressing, modulating, or augmenting immunity. Mice inoculated with avirulent transposon Tn10-mutagenized Salmonella typhimurium, χ 4062 and χ 4064 (Δcya-3 Δcrp-2 and Δcya-1 Δcrp-1, resp.), survived subsequent peroral challenge with 104 times the LD50 of fully virulent S. typhimurium SR11 χ 3306.

L5 ANSWER 51 OF 62 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN DUPLICATE 26

AN 1979:123552 BIOSIS

DN PREV197967003552; BA67:3552

TI THE PLEIOTROPIC EFFECT OF SPONTANEOUS SINGLE STEP VARIANT PRODUCTION IN MYCOBACTERIUM-INTRACELLULARE.

AU KAJIOKA R [Reprint author]; HUI J

CS CENT LAB, BOX 9000, TERMINAL A, TORONTO, ONT M5W 1R5, CAN

SO Scandinavian Journal of Respiratory Diseases, (1978) Vol. 59, No. 2, pp. 91-100.

DT Article

FS BA

LA ENGLISH

AB A strain of M. intracellulare, AT 13786, derived from human sputum, gave rise to transparent and opaque colony forms which were cloned and investigated. It was concluded that the opaque form was a mutant of the transparent type and possessed alterations in the cell envelope which were responsible for enhanced permeability. The opaque form was more susceptible to a number of antibiotics; it grew faster in standard medium, and was not dependent on Tween for dextrose utilization. Tween

enhanced the antibiotic susceptibility of the opaque form more than that of the transparent form. The avirulent opaque colony form of the pathogenic strain serotype Boone also revealed a loss of Tween dependence for dextrose utilization. The significance of the overall change was discussed with respect to the question of virulence.

L5 ANSWER 52 OF 62 CAPLUS COPYRIGHT 2007 ACS on STN DUPLICATE 27
AN 1968:417680 CAPLUS
DN 69:17680
TI Immunogenicity of cell walls from various mycobacteria against airborne tuberculosis in mice
AU Brehmer, Werner; Anacker, Robert L.; Ribi, Edgar
CS Nat. Inst. of Allergy and Infec. Dis., Hamilton, MT, USA
SO Journal of Bacteriology (1968), 95(6), 2000-4
CODEN: JOBAAY; ISSN: 0021-9193
DT Journal
LA English
AB Protective potency of oil-treated cell walls of various mycobacteria against airborne infection of mice with a few cells of Mycobacterium tuberculosis H37Rv was compared with that of viable BCG. Although less potent than BCG cell walls, the cell walls of atypical mycobacteria of Runyon groups I to IV protected against challenge by aerosol to some degree. Protection afforded by cell walls of H37Rv and of the avirulent mutants H37Ra and Washington II was comparable to that provided by BCG cell walls. However, cell walls of a highly virulent strain of M. bovis provided the best protection yet achieved. Present evidence suggests that protective substances are shared by all mycobacteria but in differing amts.; the relation between virulence and immunogenicity has yet to be clarified.

L5 ANSWER 53 OF 62 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN DUPLICATE 28
AN 1965:2683 BIOSIS
DN PREV19654600002682; BA46:2682
TI Purification and properties of the transglucosylase inhibitor of Mycobacterium tuberculosis.
AU LORNITZO, FRANK A.; GOLDMAN, DEXTER S.
CS Veterans Admin. Hosp., Madison, Wis., USA
SO J BIOL CHEM, (1964) Vol. 239, No. 9, pp. 2730-2734.
DT Article
FS BA
LA Unavailable
ED Entered STN: May 2007
Last Updated on STN: May 2007
AB Cell-free extracts of the H37Ra (avirulent) strain of M. tuberculosis contain a masked transglucosylase which catalyzes the synthesis of trehalose 6-phosphate from uridine diphosphate glucose and glucose 6-phosphate. An inhibitor of the transglucosylase is an oligoribonucleotide containing between 6 and 9 purine bases and no pyrimidine bases. The oligoribonucleotide contains guanine and adenine in a molar ratio of 21. It noncompetitively inhibits the transglucosylase, and is distinct from and is not produced by ribonuclease digestion of soluble ribonucleic-acid (RNA). The inhbitory oligoribonucleotide may be either a portion of the enzyme-forming system which accompanies the newly synthesized protein molecule or a portion of an RNA molecule which cannot be hydrolyzed during normal RNA turnover. The mutation which led to the H37Ra strain is interpreted as an alteration in the deoxyribonucleic-acid (DNA) which results in the formation either of a defective enzyme-forming system or of an RNA molecule containing a nondegradable oligoribonucleotide. ABSTRACT AUTHORS: Authors

L5 ANSWER 54 OF 62 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN DUPLICATE 29

AN 1964:29891 BIOSIS
DN PREV19644500029895; BA45:29895
TI Vitamin B12 synthesis by mycobacteria.
AU AITHAL, H. N.; SIRSI, M.
CS Indian Inst. Sci., Pharmacol. Lab., Bangalore, India
SO INDIAN JOUR EXPTL BIOL, (1963) Vol. 1, No. 3, pp. 132-134.
DT Article
FS BA
LA Unavailable
ED Entered STN: May 2007
Last Updated on STN: May 2007
AB Vitamin-B12 synthesizing ability of different strains of saprophytic, bovine and human types of mycobacteria; and the differential distribution of the vitamin-B12 activity between the culture filtrates and the bacterial mass have been investigated. No qualitative or quantitative difference in the vitamin-B12 activity of the virulent human strain (H37RV) and its avirulent mutant (H37Ra) has been observed. In general, the saprophytes exhibit greater synthesizing ability than bovine and human types. No alkali stable factors could be detected in the culture filtrates of the saprophytes, bovine and BCG strains; while about 50 percent of the vitamin-B12 activity is due to these factors in the human strains, and M. tuberculosis H37RV and M. tuberculosis. H37Ra. In the case of the human strains, there is a negligibly small amount of vitamin-B12 in the bacterial mass; while in the case of the saprophytes and the bovine types, a comparatively larger amount of the vitamin is retained in the cells. ABSTRACT AUTHORS: Authors

L5 ANSWER 55 OF 62 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
AN 1965:39451 BIOSIS
DN PREV19654600039457; BA46:39457
TI Modification of ultraviolet-induced mutation frequency and survival in Mycobacterium avium by pre-irradiation incubation in phosphorus-deficient medium.
AU TSUKAMURA, MICHIO
CS Obuso Nat. Sanatorium, Obu, Aichi, Jap.
SO JAP J MICRO BIOL, (1963) Vol. 7, No. 3, pp. 97-104.
DT Article
FS BA
LA Unavailable
ED Entered STN: May 2007
Last Updated on STN: May 2007
AB Effects of pre-irradiation treatments on the ultraviolet-induced mutation frequency and survival were investigated in an avirulent strain (Jucho strain) of Mycobacterium avium. Pre-irradiation incubation in phosphorus-deficient medium gave rise to an increase in sensitivity to ultraviolet irradiation when this pre-treatment itself caused no viability damage. Post-irradiation incubation in a medium supplemented with phosphates did not recover the loss in viability caused by ultraviolet irradiation in the cells pre-incubated in phosphorus-deficient medium. The increase of ultraviolet sensitivity was compatible with the previous finding in that ultraviolet irradiation produced a significant liberation of radioactive phosphorus compounds during irradiation. Pre-irradiation incubation of cells in phosphorus-deficient medium promoted a marked decline in ultraviolet-induced mutation frequency to streptomycin resistance, while it caused no decline in induced mutation frequency to isoniazid resistance. Possibly phenotypic expression of mutation to streptomycin resistance requires sufficient amount of some phosphorus compounds. Pre-irradiation incubation in nitrogen-free medium also caused increase in ultraviolet sensitivity. ABSTRACT AUTHORS: Author

L5 ANSWER 56 OF 62 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on

STN DUPLICATE 30

AN 1963:19220 BIOSIS
DN PREV19634100019221; BA41:19221
TI Enzyme systems in the myco-bacteria. XII. The inhibition of the transglycosidase-catalyzed formation of trehalose 6-phosphate.
AU GOLDMAN, DEXTER S.; LORNITZO, FRANK A.
CS Vet. Admin. Hosp., Madison, Wis., USA
SO JOUR BIOL CHEM, (1962) Vol. 237, No. 11, pp. 3332-3338.
DT Article
FS BA
LA Unavailable
ED Entered STN: May 2007
Last Updated on STN: May 2007
AB Cell-free extracts of several strains of Mycobacterium tuberculosis contain a transglycosidase that catalyzes the formation of trehalose 6-phosphate from glucose 6-phosphate and uridine diphosphate-glucose. The specific activity of the enzyme of a virulent strain of M. tuberculosis is considerably higher than that of its avirulent mutant. The low activity in the avirulent strain is due to inhibition of the trans -glycosidase activity. The non-competitive inhibitor is active against both avirulent and virulent mycobacteria. The avirulent strain may be freed of the inhibitor by isoelectric precipitation. The transglycosidase separated from the inhibitor shows approximately the same specific activity as that in virulent strains of the tubercle bacillus. ABSTRACT AUTHORS: Authors

L5 ANSWER 57 OF 62 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
AN 1965:39450 BIOSIS
DN PREV19654600039456; BA46:39456
TI Mutations and inactivation of mycobacteria induced by ultraviolet irradiation.
AU TSUKAMURA, MICHIO
CS Obuso Nat Sanatorium, Obu, near Nagoya, Aichi-pref, Jap.
SO JAP J TUBERC, (1962) Vol. 10, No. 1/2, pp. 1-14.
DT Article
FS BA
LA Unavailable
ED Entered STN: May 2007
Last Updated on STN: May 2007
AB Resting cells of M. tuberculosis var. hominis, strain H37Rv, and avirulent strains of M. avium, strains S-type Jucho, R-type Jucho and Takeo, were exposed to ultraviolet radiation. These strains yielded dose-survival curves of a single-hit type supporting the one nucleus theory rather than the multinuclei theory of mycobacteria. The dose-mutation curves showed a marked discrepancy between mutations to streptomycin resistance and to isoniazid resistance in the H37Rv strain. During irradiation, the mutation frequency to isoniazid resistance increased rapidly, while the mutation frequency to streptomycin resistance increased only slowly. This discrepancy was also observed but to a lesser extent in the S-type Jucho strain. The existence of the discrepancy appears to be strain-specific. Phenomic lag was found for the expression of mutation to streptomycin resistance in the Jucho strain, while it was not found in the mutation to isoniazid resistance. In the H37Rv strain, both mutation frequencies were increased by the post-radiation incubation. Induced mutation to streptomycin resistance in the S-type Jucho strain was almost completely eliminated by post-treatment with chloramphenicol, while induced mutation to isoniazid resistance remained almost unchanged by the same treatment. Ultraviolet-resistant strains of mycobacterium were found to be only transient and they exhibited a single-hit survival curve. It was suggested that these transient radiation-resistant strains are of

cyto-plasmic origin. ABSTRACT AUTHORS: Author

L5 ANSWER 58 OF 62 CAPLUS COPYRIGHT 2007 ACS on STN
AN 1962:74781 CAPLUS
DN 56:74781
OREF 56:14591e-f
TI Comparison of effects of atom decay and beta-ray radiations on the inactivation and mutation of a mycobacterium
AU Tsukamura, Michio
CS Obuso Natl. Sanatorium, Obu, Japan
SO Genetics (1961), 46, 1561-4
CODEN: GENTAE; ISSN: 0016-6731
DT Journal
LA Unavailable
AB The effects of P32 and Sr90 (added to culture medium) on an avirulent strain of Mycobacterium avium were compared. Addition of 1 μc. P32/ml. to culture medium caused both inactivation and mutation. Addition of 20 μc. Sr90/ml. caused some increase of mutations and no inactivation. Addition of 2 μc. caused no increase in mutations. Results suggested that decay of P32 atoms incorporated into cells cause inactivation and mutation.

L5 ANSWER 59 OF 62 CAPLUS COPYRIGHT 2007 ACS on STN
AN 1960:119136 CAPLUS
DN 54:119136
OREF 54:22837c-d
TI Relation between the intracellular localization of beta-radioisotopes and their mutagenic effect
AU Tsukamura, Michio
CS Obuso Natl. Sanatorium, Obu, Aichi-ken
SO Genetics (1960), 45, 309-14
CODEN: GENTAE; ISSN: 0016-6731
DT Journal
LA Unavailable
AB Mycobacterium avium, strain Jucho (avirulent) cells were inoculated into liquid modified Sauton medium containing 0.5 μc. of P32 orthophosphate/ml. of medium, or into a S-deficient liquid Sauton medium containing 10 μc. of sulfate-S35/ml. of medium. Ratios of streptomycin-resistant mutants and isoniazid-resistant mutants were used as markers of mutation frequencies. A 10-fold increase of mutation frequency occurred in cells irradiated by P32. No increase occurred in S35 irradiated cells although uptake of S35 was greater than P32 uptake. The mutagenic effect may be due to the intracellular localization of the P32 isotope.

L5 ANSWER 60 OF 62 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
AN 1960:50890 BIOSIS
DN PREV19603500050912; BA35:50912
TI Sulfolipid from virulent tubercle bacilli.
AU MIDDLEBROOK, G.; COLEMAN, C. M.; SCHAEFER, W. B.
CS Natl. Jewish Hosp., Denver, Colorado
SO PROC NATL ACAD SCI, (1959) Vol. 45, No. 12, pp. 1801-1804.
DT Article
FS BA
LA Unavailable
ED Entered STN: May 2007
Last Updated on STN: May 2007
AB The bacterial cells of pathogenic human and bovine varieties of Mycobacterium tuberculosis fix the dye, neutral red, to their surface while attenuated or avirulent mutant strains do not. Analysis of the material responsible for this is described and evidence presented that the material contains a high proportion of methyl groups suggestive of methyl-branched-chain fatty acids, it has few

alcoholic hydroxyl groups, the infrared spectro-photometric absorption bands at 1020-1060 cm-1 and 1140-1200 cm-1 are consistent with those of a sulfonic acid, it lacks carbon-to-carbon unsaturated bonds and has no phthienoic type of fatty acid, and contains a prominent carboxylic acid ester absorption band and little or no free carboxylic acid. These studies and others made on other selected strains are described in detail. ABSTRACT AUTHORS: J. S. Greenstein

L5 ANSWER 61 OF 62 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
AN 1955:21681 BIOSIS
DN PREV19552900021735; BA29:21735
TI The mycolic acids of three human strains of Mycobacterium tuberculosis: H-37 Ra H.37 Rv and a streptomycin-resistant mutant of H-37 Rv.
Original Title: Sur les acides mycoliques de trois souches humaines de Mycobacterium tuberculosis: H-37 Ra, H-37 Rv et un mutant H_37 Rv streptomycino-resistant.
AU ASSELINEAU, J.; GENDRE, T.
CS Inst. Biol. Physico-Chim., Paris
SO BULL SOC CHIM FRANCE, (1954) Vol. 1954, No. 10, pp. 1226-1233.
DT Article
FS BA
LA Unavailable
ED Entered STN: May 2007
Last Updated on STN: May 2007
AB Isolation of 11 mycolic acids from the avirulent strain H.37 Ra and the virulent strains H-37 Rv and H-37 Rv S.r. (a mutant which is streptomycin-resistant) is described. Existence of 2 kinds of mycolic acids with 3 atoms of O2 was established. A certain number of derivatives of each of these acids was prepared. The chromic acid oxidation of the dihydroxy acids, alpha2 and beta mycolic acids, led to different diketones. In the alpha2-mycolic acid from H-37 Rv and the beta-mycolic acid from H-37 Rv (S.r.), one hydroxyl is in position 3 and the other in position 6 or beyond. ABSTRACT AUTHORS: I. E. Liener

L5 ANSWER 62 OF 62 CAPLUS COPYRIGHT 2007 ACS on STN
AN 1951:16960 CAPLUS
DN 45:16960
OREF 45:3029b-e
TI Differences in response of a virulent strain of the tubercle bacillus and its avirulent variant to metabolites and their genetic significance
AU Marshak, Alfred
SO Journal of Bacteriology (1951), 61, 1-16
CODEN: JOBAAY; ISSN: 0021-9193
DT Journal
LA Unavailable
AB Of various amino acids (AA) tested, 13 had no significant effect on the rate of growth of either H37Ra or H37Rv strain of mycobacteria. The rate of growth of each strain was increased by 6 AA, but only α-alanine stimulated 1 strain (H37Ra) and not the other. Two AA inhibited both strains and 4 inhibited only H37Rv. Of 17 other metabolites studied, only thymine, hypoxanthine, and nicotinic acid had a differential inhibitory effect and none caused stimulation. Adenosine inhibited growth completely and caused lysis. When adapted to adenosine, H37Ra quantitatively converted adenosine to inosine. The latter was not inhibitory and apparently not utilized. Adenine inhibited both strains to a lesser degree than adenosine, which may be due to its competition with adenosine triphosphate, rather than interference with nucleic acid metabolism. Only methionine and choline antagonized the adenine-induced inhibition, and this primarily with H37Rv. It is postulated that the 2 strains differ in that H37Ra has lost the capacity to utilize phospholipides, also that H37Rv uses at least 2 pathways for acetylation,

whereas H37Ra retains only that which involves condensation of AA with pyruvate. H37Ra and H37Rv may differ by a single gene mutation. 47 references.